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The Clinical Significance of Leucopenia with Special Reference to Idiopathic Neutropenia

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THE development of leucopenia without apparent cause in a previously healthy individual is a subject about which there has been considerable discussion in recent years. Leucopenia brought on by definite etiologic factors such as certain bacterial and protozoan infections, toxic chemicals, or destruction of the bone marrow by tumor processes is readily understandable. Here the problem is concerned chiefly with diagnosis, and eradication or alleviation of the primary cause. There are instances of leucopenia, however, that are not so readily explained, and in which the cause remains obscure. In the medical literature one may find such conditions designated as "granulopenia", "granulocytopenia" of unknown origin, or "idiopathic" neutropenia. Cases of leucopenia falling in this group warrant further investigation. During the past three years we have had opportunity to observe several cases of leucopenia of this nature, and certain of these will be discussed in this paper.

Before discussing the clinical aspects of leucopenia, it is necessary to consider the polymorphonuclear leucocyte, its origin and various stages of development from youth to maturity. The progenitor of the granulocyte series is a cell in regard to the exact identity of which there still remain differences of opinion. The concept of Sabin[1] and her associates on leucogenesis, however, has somewhat clarified the situation, and offers a tenable hypothesis on cell development from the primitive form to maturity. Whether or not the erythrocyte and granulocyte arise from a common parent cell, it is generally accepted that leucopoiesis normally takes place outside the blood sinusoids of the bone marrow, and the granulocytes gain entrance to the capillaries through their own motility. According to the concept of Sabin, the primitive progenitor of the granulocyte arises from a reticular cell lining the sinusoids of the bone marrow, and from this stage passes through an orderly transformation to the adult form. The next cell in order is the myeloblast,

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and from this point on, maturation is a matter of cellular differentiation consisting in nuclear indentation and lobulation. As the cells age, cytoplasmic inclusions appear and their presence and tinctorial differences may be detected through the use of appropriate stains. In the bone marrow the young granular forms are designated as myelocytes a, b, and c, and the metamyelocyte. Normally in the circulation the fully matured form of the granulocyte appears as the motile, polymorphonuclear leucocyte.

When the bone marrow becomes involved by disease, leucopoiesis is interfered with, and under certain conditions leucopenia develops. Improper growth, failure of development, and aplasia of the bone marrow may appear as intrinsic disorders, and the white blood cells, the red blood cells, and the platelets become reduced in number. On the other hand, there are conditions in which the bone marrow shows marked cellular overgrowth of the leucocytic series, but apparently there is retarded maturation and the granulocytes in the blood become reduced.

This brief review is essential to the proper understanding of the pathologic physiology of the cases to be presented.

In an effort to obtain some information concerning the clinical significance of leucopenia, its relation to various clinical conditions, and conditions of occurrence of benign leucopenia, a statistical study of 10,000 hospital records was undertaken. A summary of the observations is presented here in the form of tables, and certain deductions are made from the figures obtained.

In order to divide properly the 10,000 cases into a leucopenic group, those with normal, and those with elevated leucocyte counts, the figure of 5,000 leucocytes per c. mm. of blood was accepted as being the low standard for normal. In most text books of medicine it is stated that individuals in whose blood there are found 5,000 leucocytes or less per c. mm. show a state of leucopenia.

Frequency and Conditions of Occurrence of Leucopenia

There are few data available that concern directly the frequency of leucopenia. Roberts and Kracke[2], in a statistical study of 8,000 records of patients seen in private practice for the ten-year period between 1920 and 1930, recorded that leucopenia occurred in 1,881 or 23 per cent of their patients. These authors took 6,000 leucocytes per c. mm. of blood as the lower limit of normal.

The data to be presented have been derived from the records, exclusive of the outpatient department, of the University of California Hospital. Examination of the records was limited to those belonging to the Division of Medicine, and the results obtained, therefore, represent a cross section of the illnesses suffered by the patients entering a general medical service. Patients who were in for "overnight" observation or treatment, and in whose records there does not appear an adequate history, the results of a complete physical examination or the reports of the "routine" laboratory tests are excluded from this series.

From January, 1920, until January,

1931, 10,000 case records were made and these form the basis of this study. A high percentage of the patients presented a definite diagnostic problem that required analysis through careful physical examination and laboratory studies. Accordingly, in the records of patients in whose blood there was found an inadequate number of leucocytes, there usually appeared two or more leucocyte counts. An analysis of the blood reports of 1,167 of the total number of patients showed leucocyte counts of 5,000 cells or less per c. mm. Thus, 11.67 per cent of the patients entering the medical wards during the eleven-year period were deficient in white blood cells.

In table I have been summarized the cases of leucopenia occurring in the medical records of the University of California Hospital, together with the percentage frequency of occurrence among the various disorders.

TABLE I

Number of Records Examined	10,000
Number with Leucopenia	1,167
Females with Leucopenia	611—52.4 per cent of cases
Males with Leucopenia	556—47.6 per cent of cases

CONDITION IN WHICH LEUCOPENIA OCCURRED	NUMBER OF CASES WITH LEUCOPENIA	PER CENT INCIDENCE OF LEUCOPENIA IN THE VARIOUS CONDITIONS
I		75 TO 100 PER CENT INCIDENCE
Influenza	137	100 per cent of cases
Typhoid fever	14	100 " " " "
Brucelliasis (undulant fever)	7	100 " " " "
Banti's disease (splenic anemia)	19	100 " " " "
Aleukemic leukemia	9	100 " " " "
Aplastic anemia	5	100 " " " "
"Agranulocytic" angina	2	100 " " " "
Arsphenamine intoxication	2	100 " " " "
Pernicious anemia, in relapse	109	97 " " " "
Malaria	29	82 " " " "
Myxedema untreated	30	75 " " " "
II		25 TO 75 PER CENT INCIDENCE
Sprue	4	57 per cent of cases
Hodgkin's disease	23	52 " " " "
Arthritis, acute infectious	6	33 " " " "
Jaundice, catarrhal	9	31 " " " "
Cirrhosis of liver	22	26 " " " "
Endocarditis, subacute bacterial	13	25 " " " "
Lymphosarcoma	6	25 " " " "
III		4 TO 25 PER CENT INCIDENCE
Septicemia, staphylococcus	2	22 per cent of cases
Hyperplasia of thyroid gland	54	22 " " " "
Hemolytic jaundice, acquired	3	11 " " " "
Tuberculosis (all forms)	57	21 " " " "
Cholecystitis, chronic	60	17 " " " "
Lead poisoning	3	13 " " " "
Rheumatic valvulitis, chronic	18	12 " " " "
Infectious mononucleosis	1	15 " " " "
Arthritis, chronic infectious	9	10 " " " "
Peptic ulcer	34	10 " " " "
Lues (tertiary)	41	9.7 " " " "
Arthritis, chronic hypertrophic	20	7.6 " " " "
Diabetes mellitus	36	7.4 " " " "
Pellagra	1	4 " " " "

IV

MISCELLANEOUS

Conditions in which the Per Cent Incidence of Leucopenia was not Determined Because of Difficulties Encountered in Classification

	NUMBER OF CASES WITH LEUCOPENIA
Neoplasms (all forms)	114
Arteriosclerosis	58
Tonsillitis, chronic	17
Colitis, chronic	13
Appendicitis	11
Nephritis, chronic	11
"Secondary" anemia	11
Cystitis, chronic	7
Sinusitis, chronic	6
Bronchitis, chronic	5
Thrombocytopenic purpura	5
Bronchopneumonia	2
Osteomyelitis, chronic	2
Measles (adult)	2
Peritonitis, chronic	1
Dysentery, amebic	1
Dysentery, bacillary	1
Allergy	1

V

UNEXPLAINED LEUCOPENIA

No diagnosis	70 cases 6 per cent of all cases of leucopenia
Nervous exhaustion Neurosis, psychosis, hysteria	44 cases 3.7 per cent of all cases of leucopenia

From an examination of the table it will be noted that 52.4 per cent of the total number of cases of leucopenia occurred in females and 47.6 per cent of the cases in males. This indicates a moderately increased incidence of leucopenia in the female sex.

Data relative to the various conditions and different states of ill health in which leucopenia may be found of less frequent occurrence are listed in groups II, III, and IV. It will be observed that leucopenia occurred in very high incidence in a rather limited number of diseases set forth in group I. Of some interest is the appearance of numerous instances of leucopenia in patients with chronic disorders of one sort or another.

Clinically, the division of the idiopathic or obscure leucopenias into well defined groups presents a great difficulty because of lack of knowledge of the etiologic factors concerned. However, there are cases of severe leucopenia that persist over a period of weeks or months. These are usually associated with other abnormalities of hematopoiesis, and are frequently fatal. These may be differentiated from cases in which the abnormality of leucopoiesis is less severe in degree. With these facts in mind two clinical groups of leucopenia of obscure origin may be defined:

I Malignant leucopenia of obscure origin,

II Benign leucopenia of obscure origin.

Malignant Leucopenia of Obscure Origin

The following cases are illustrative examples of conditions falling into this group:

Case I, Idiopathic Aplastic Anemia.* J. L. T., a white, married, American farmer, aged 27, entered the hospital September 12, 1928, complaining of weakness and pallor. Except for pertussis at 6 years of age, chicken pox at 11, measles at 17, and bilateral mumps at 23 years of age, he had enjoyed good health for four years until the latter part of May, 1928. At that time a localized infection appeared on the back of his right hand, which, with surgical intervention, healed at the end of 3 weeks. About a month later, he began having signs and symptoms of anemia. A week prior to entry, small ecchymoses appeared on his legs following trivial trauma. He lost 10 pounds in weight during the month of June. The patient was undernourished and very pale. There were fading ecchymoses over both tibiae. Physical examination revealed no other abnormality.

Laboratory data. The examination of the blood on September 12 showed: erythrocytes, 1,216,000 per c. mm.; hemoglobin, 29 per cent (S); color index, 1.2; hematocrit, 15 per cent of cells; reticulocytes, 0.4 per cent with a comparable number of polychromasic cells. There were an occasional large and a few small erythrocytes. A few red blood cells were oval in shape and a few showed central pallor. The leucocytes numbered 2,500 per c. mm. of blood. Differential count: polymorphonuclears, 24 per cent; lymphocytes, 70 per cent; monocytes, 6 per cent. The platelets were greatly reduced. The bleeding time was 15 minutes. The coagulation time by the method of Lee and White was 15 minutes. No clot retraction occurred at the end of 3 hours at 37°C.

The basal metabolic rate was plus 6.5 per cent. The Kahn test on the blood serum was negative. Repeated blood cultures revealed no bacterial growth. Fractional gastric analysis showed the presence of free hydrochloric acid in normal amount.

A biopsy of sternal marrow was performed on September 13. This tissue was made up largely of fat cells. Small focal hematopoietic clusters of cells were scattered between the interstices of those cells, and only in one area was there a focus of apparent cellular activity as shown in figure 1. In these foci there were a moderate

*It is a pleasure to record our thanks to Doctor George R. Minot for the opportunity to study cases I and II at the Thorndike Memorial Laboratory of the Boston City Hospital, and to Doctor Frank B. Mallory of that hospital for the use of the autopsy material.

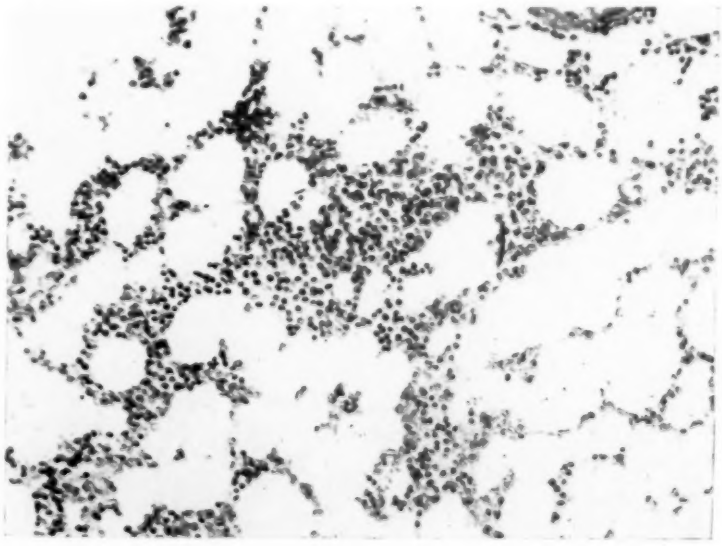

FIG. 1. Specimen of bone marrow removed at biopsy from sternum of patient in case I. Note small focus of hematopoiesis in an otherwise aplastic bone marrow.

number of neutrophilic myelocytes and an occasional eosinophilic myelocyte, but in the entire specimen no adult granulocytes nor megakaryocytes were observed. The cells comprising the foci were chiefly erythroblasts and myeloblasts, among which an occasional mitotic figue was noted. The endothelial cells lining the sinusoids in the areas of hematopoiesis were of moderate size, but were small in the collapsed sinusoids. A few large phagocytic cells containing pigment were seen. Diagnosis: Aplastic bone marrow.

Course of illness. On September 19, small hemorrhages appeared in the retinae and the following day small petechiae were visible in the skin over different parts of the body. On September 22, 1928, the patient was given his first transfusion of blood. Liver pulp in amounts of 300 grams daily for a period of 10 days and a subsequent course of liver extract 343 N. N. R., derived from 600 grams of liver daily, failed to affect the bone marrow. Temporary relief was afforded by 6 transfusions of blood, 3 of which were given on 3 successive days prior to splenectomy. During the two and one-half months the patient was in the hospital, examinations of the blood were made at frequent intervals. The erythrocytes fluctuated between 600,000 and 1,000,000 per c. mm., depending chiefly upon transfusions of blood. The reticulocytes varied from 0.4 and 1.0 per cent. The leucocyte count varied from 1,700 to 2,500 per c. mm. The differential count remained essentially the same as at entry. On November 11, 1928, splenectomy was performed notwithstanding the diagnosis of aplastic anemia; there was a forlorn hope that the operation might favorably affect the patient. The spleen weighed 128 grams. Microscopical examination showed it to be normal except for slight enlargement of the malpighian bodies.

A week after splenectomy, petechial hemorrhages reappeared over the body. The patient began to have frequent severe nosebleeds, grew steadily paler and weaker, and died November 28.

The autopsy showed an aplastic, fatty bone marrow, an area of chronic organized and interstitial pneumonia in the middle lobe of the right lung, and generalized petechiae.

Discussion

In this case, idiopathic aplastic anemia occurred in a previously healthy adult male 27 years of age. Neither exposure to overdoses of x-ray, radium, benzol, or arsenicals, nor some hidden focus of infection could be held as an etiological factor. The condition appeared to be an intrinsic abnormality of hematopoiesis, and failure in leucocyte, erythrocyte, and platelet production.

Of some importance, however, is the fact that apparently active but small foci of blood formation could be seen in the specimens of bone marrow removed at biopsy, an example of which is shown in figure 1. Among such clusters of cells a few mitotic figures were noted. Similar observations have been recorded by Mills.[3] This evidence of hematopoietic activity holds forth hope of discovery of some substance, the administration of which will permit adequate erythrocyte and leucocyte growth.

Case II, Agranulocytosis, Esophagitis. I. W. S., a Jewish housewife, aged 47 years, was brought to the hospital on May 11, 1929, suffering from weakness, headaches, chills and fever. One of her mother's sisters had died of Hodgkin's disease at 50 years of age. During childhood the patient had "black" measles, mumps, chickenpox, smallpox, and scarlet fever. It was stated that she had had typhoid fever at 14 years of age, and dengue fever at 40. Eleven years before the present illness, an abscess developed in the right breast following childbirth. Tonsillectomy was done 10 years before, at which time she lost "much blood." All her upper teeth were removed 9 years before.

The patient said she had been "anemic all her life." About 1916 her blood was reported to show slight anemia. Two years before death she received a series of iron and arsenic injections after which she felt better.

During the winter of 1928 and 1929 she had been as well as usual, but suddenly on the evening of April 14, 1929, she experienced "chills and fever," when she "shook all over". Severe headache accompanied this attack. Her temperature was 101°F. The next day she felt quite well. Similar attacks occurred on April 24, 30, and May 6. The last attack was the most severe, and the headache persisted 4 days. The height of the fever was between 103° and 104°F.

On April 25, 1929, examination of the blood by her physician showed the following: erythrocytes, 3,750,000 per c. mm.; hemoglobin, 58 per cent; leucocytes, 9,000 per c. mm.; polymorphonuclear leucocytes, 75 per cent.

On May 1, 1929, the leucocytes were 2,500 per c. mm.; polymorphonuclear leucocytes, 40 per cent; lymphocytes, 60 per cent.

The patient, on hospital entry, May 11, 1929, appeared well-nourished, and quite comfortable.

Physical examination. There was moderate pallor of the skin and mucous membranes. There was no apparent ulceration of the pharyngeal structures. No enlarged lymph nodes could be felt. The spleen was palpable only on deep inspiration. The liver edge was easily felt.

Laboratory data. Examination of the blood on May 13, 1929, showed: erythrocytes, 3,400,000 per c. mm.; hemoglobin, 76 per cent (S); hematocrit, 45 per cent of cells; leucocytes, 1,200 per c. mm.: differential count: polymorphonuclear leucocytes, 6 per cent; monocytes, 32 per cent; large lymphocytes, 28 per cent; small lymphocytes, 32 per cent; young lymphocytes, 2 per cent. Several red blood cells showed polychromatophilia and stippling, and there was slight anisocytosis and poikilocytosis. The platelets appeared in normal numbers. There were 1.2 per cent of reticulocytes.

X-ray examination of the gall bladder failed to reveal stones or any abnormality in the function of this organ. The Wassermann and Kahn tests were negative.

Between May 16 and 29 daily stool examinations were strongly guaiac-positive for blood, but were negative for parasites or ova. Stool cultures were negative for pathogenic bacteria. Several blood cultures showed no bacterial growth.

Examination of the blood on May 20, 1929, showed: erythrocytes, 3,450,000; hemoglobin, 76 per cent (S); leucocytes, 1,800 cells per c. mm.: differential count: supravital stain, polymorphonuclear leucocytes, 0; small lymphocytes, 33 per cent; large lymphocytes, 32 per cent; monocytes, 35 per cent. The monocytes were sluggishly motile and contained large multilobulated nuclei. Most of these cells were oxidase negative with the peroxidase stain.

The patient gradually grew worse, became comatose and died on May 20, 1929.

Postmortem examination. Autopsy was performed 2½ hours after death. There was a pale yellow tint to the skin and sclerae. The appendix and a few loops of adjacent small intestine were bound together by fibrous tissue. The liver edge projected 11 cms. below the tip of the xiphoid and 6 cms. below the right costal margin. The mesenteric lymph nodes were not enlarged. Positive findings follow:

Spleen: Weighed 240 grams (about twice normal size). The surface was dark gray-purple, and the capsule irregularly thickened. The freshly cut surface was dark red and showed fairly prominent trabeculae. Very little pulp scraped away.

Gastro-intestinal tract: The lower one-third of the esophageal wall and adjacent 2 centimeters of stomach were moderately thickened and the mucosa had a light brown, parboiled appearance. It could be rubbed off with ease. Remaining intestinal tract was negative.

Liver: The liver weighed 2,200 grams. It was normal in shape and consistency. There were numerous fibrous tags on the upper surface. The freshly cut surface was red-brown with indistinct markings. The gall bladder was thin-walled and contained a small amount of normal-appearing bile.

Bone marrow: The bone marrow of the vertebrae and sternum was red in appearance and of normal consistency. In the femur it was red in the upper two-thirds and mostly fat tissue in the lower third.

Microscopic examination. Esophagus: The wall was congested and showed extensive lymphocytic infiltration and edema. Numerous endothelial leucocytes and small masses of fibrin were also present. The mucosa and submucosa were necrotic, partly desquamated

and invaded by large numbers of bacteria and fungi. Among the bacteria, cocci and medium-sized baccili were most numerous. Long, slender, branching forms resembling streptothrix were also present, especially in the deeper portions of the submucosa.

Stomach: A specimen from the cardiac portion of the stomach showed diffuse infiltration with lymphocytes and plasma cells.

Spleen: There was slight increase in connective tissue throughout. A few follicles contained central masses of fibrin. There were several small, round well-encapsulated pink staining masses in which no structure could be made out.

Liver: There was slight lymphocytic infiltration of the portal spaces. There were several small homogeneous pink staining masses similar to those in the spleen.

Bone Marrow: A specimen of bone marrow from the upper third of the right femur showed a slightly increased amount of fat. The cells of the hematopoietic centers were diminished in numbers. No polymorphonuclear leucocytes were to be seen. There were numerous promyelocytes with large single nuclei, and faintly neutrophilic cytoplasm. No definite neutrophilic nor eosinophilic myelocytes could be distinguished. There were normal-appearing foci of erythropoiesis. A fairly good number of megakaryocytes was seen. There was a scattering of lymphocytes and plasma cells.

Discussion

The observation of Schultz[1] in 1922 of a group of patients whose clinical pictures were those of leucopenia associated with sepsis resulted in an attempt at formulation of a new clinical entity. This condition has become known as agranulocytosis, agranulocytic angina, malignant neutropenia, idiopathic neutropenia, and by other descriptive terms. In the past it has been customary to attribute the leucopenia to the necrotizing process, sepsis or some "toxic" factor and most of the cases have been studied from that point of view. In recent years it has become more and more apparent that the disease may not be an entity as was first supposed but more probably a syndrome. The reason for this change in thought is that the composite clinical picture, which is frequently present, is now known not to be associated with a single or specific type of infectious process, but may be found in the presence of a variety of septic conditions as have been reported by Blumer,[3] Roberts and Kracke,[2] Thompson,[6] Rose and Hauser[7] and others.

This concept of granulocytopenia occurring as a manifestation of multiple clinical disorders in man is an important one, and has suggested to Rosenthal,[8] among others, that there may be a leucopenic predisposition or trend in certain individuals. During the life of this patient she was beset with a multiplicity of unrelated types of infection. Terminally there was a profound and persistent idiopathic neutropenia which was found at autopsy to be associated with an esophagitis and gastritis.

The bone marrow in this patient appeared fundamentally different from that in the previous patient. Here there was evidence of adequate platelet and red blood cell production from their precursors in the bone marrow, but it seemed apparent that leucopoiesis was retarded or impaired at the promyelocyte stage.

The recent publication of Jackson[9] and his associates on the use of a pentose nucleotide (nucleotide K-96) for use in cases of malignant neutropenia associated with infection offers some encouragement in the treatment of this disease.

We wish to report a case of neutro-

penia associated with infection in which recovery occurred during the course of administration of nucleotide K-96. No definite conclusions can be drawn as yet with regard to the efficacy of this therapeutic agent until a large number of cases have been studied. The course taken by the leucocytes in the patient reported below is given in figure II.

Case III, Staphylococcus Lymphangitis with Leucopenia; Patient's Subsequent Recovery. S. R. (Hospital No. 64,717), a white American housewife, aged 52 years entered the hospital February 29, 1932. She stated that one week prior to hospital entry she had received a slight burn on the anteroradial aspect of the left wrist. This was followed by scab formation, and so far as she knew, the lesion was healing. The day before entry, the patient noticed for the first time "red streaks" extending up the anterior and medial aspects of the left forearm.

Her past history was unimportant except that in childhood she had mumps, pertussis, and measles. Twenty years ago she had an abscess in the left hand that had promptly healed. During the past year she had been under the care of a physician for arterial hypertension.

Physical examination. The patient was well-nourished and developed. There was no apparent ulceration of the pharyngeal structures. No enlarged superficial lymph nodes could be felt. Neither the spleen nor the liver were found enlarged on palpation. The blood pressure was 170 systolic, and 80 diastolic. There was a small, slightly elevated, round, hyperemic lesion on the radial aspect of the left wrist. No purulent material was visible. Extending up the forearm were numerous red and enlarged lymphatic vessels. The patient's temperature was 38.4°C.; the respiration rate, 24 per minute; and the pulse beat, 120 per minute.

Laboratory data. Examination of the blood on February 29, 1932, showed: erythrocytes, 4,600,000; hemoglobin, 85 per cent (S); leucocytes, 8,600 cells per c. mm.: differential count: polymorphonuclear leucocytes, 78 per cent; polymorphonuclear basophiles, 1 per cent; lymphocytes, 16 per cent; monocytes, 5 per cent. The platelets appeared slightly increased in number. Several blood cultures showed no bacterial growth. Cultures obtained on two occasions from the inflammatory process on the left wrist were reported to contain *Staphylococcus aureus.* Soon after entry, the patient's left arm was placed in a hot magnesium sulphate bath for two hours. This procedure was carried out twice daily.

Course of illness. On the third day of the patient's stay in the hospital, her leucocytes were found to number 800 per c. mm. and the following day, 400 per c. mm. Nucleotide (K-96) in amounts of 10 c.c. was administered intramuscularly twice daily for 9 days. Beginning about the fifth day after the initial injection of nucleotide, an increase in the number of polymorphonuclear leucocytes became apparent in the peripheral circulation. On the eleventh day of this treatment, the leucocytes were 10,050 per c. mm. of blood. Coincident with the increase in the number of leucocytes there was a lessening in the severity of the patient's infection. Fifteen days after the patient entered the hospital there was a complete disappearance of the inflammatory process and the patient's temperature had returned to normal. In figure 2 are recorded the temperature and blood counts of the patient together with the time interval during which nucleotide was administered.

Case IV, Aleukemic Myeloblastic Leukemia with Chloroma.* E. L. M. (Hospital No. 59,836), a four-year-old white female was admitted to the Pediatric Service of the University of California Hospital February 18, 1931, because of pallor and weakness of six weeks' duration. In the past she had had pertussis at 2 years of age, followed soon after by a severe attack of scarlet fever. This was complicated by otitis media. The patient was a fat, rosy-cheeked girl until November 1, 1930, when she developed a "cold" with serous nasal discharge. This "cold" failed to respond to treatment, and about the middle of November the child's color had become pale. She had also become weak and was forced to spend most of the day in bed. During January, 1931, dyspnea

*We wish to thank Doctor Francis S. Smyth for permission to study this case.

became noticeable upon exertion. About the middle of January, a swelling of the frontal portion of the skull appeared just above the nose, and both eyes began to appear more prominent than previously. Physical examination on admission disclosed an undernourished, pale child who was obviously ill. There was no evidence of rash or petechiae in the skin. All superficial lymph glands were slightly enlarged, discrete and firm. The anterior fontanel was open and the anterior sutures were separated. The forehead, just above the bridge of the nose, bulged over an area of about 3 by 3 inches, and the veins in this area were slightly more prominent. A loud bruit, synchronous with the pulsation of the temporal artery, was heard over this area. There was bilateral exophthalmos, most marked on the right. Ophthalmoscopic examination showed bilateral choked discs of 1 to 1½ diopters. There were a few scattered retinal hemorrhages of small size. The heart and lungs were normal. The liver edge was felt 2 cms. below the right costal margin, and the spleen was felt 3 cms. below the left costal margin. The laboratory data showed: a hemoglobin of less than 20 per cent (S); the red blood cells were 840,000 per c. mm.; and the white blood cells, 1,550 per c. mm. In the differential count, using the supravital staining technic, there were polymorphonuclear leucocytes, 31 per cent; large lymphocytes, 12 per cent; small lymphocytes, 16 per cent; myelocytes, A, 1 per cent, B, 5 per cent, C, 25 per cent; monocytes, 10 per cent. Tests for bleeding time and clotting time showed these functions to be within normal limits. The blood Wassermann reaction was one plus. X-ray examinations of the long bones and ribs were negative and there was no evidence of bony destruction in the skull, but there were signs of increased intracranial pressure. Blood cultures failed to produce any bacterial growth.

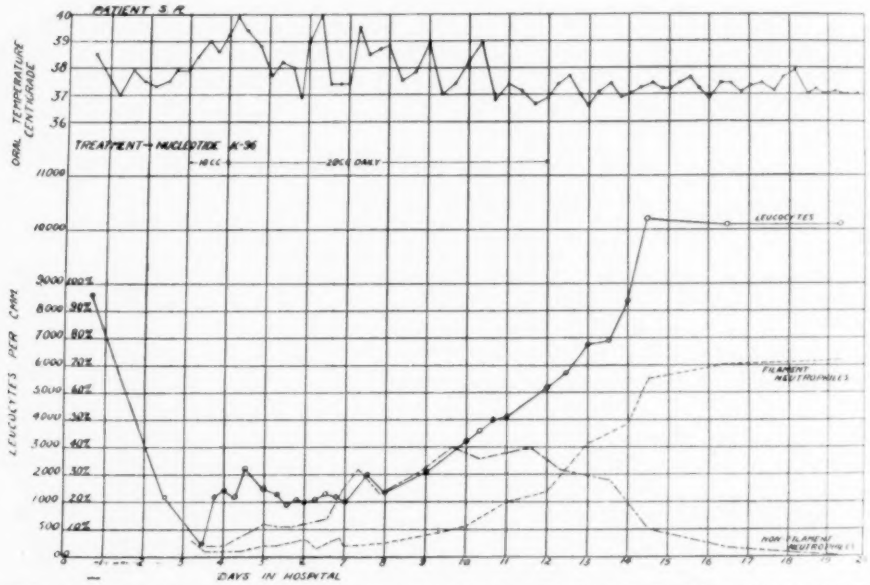

FIG. 2. The occurrence of leucopenia in a female patient with lymphangitis of the arm followed by recovery during the intramuscular administration of nucleotide K-96.

Course of illness. Following exposure to the x-ray on five different occasions, the mass in the frontal region of the skull diminished in size and the exophthalmos receded. Her strength and appearance were improved by six transfusions of whole blood in amounts of 300 c.c. On March 22, 1931, a few days after the last x-ray treatment, a fever of 40°C. was noted, and petechial

hemorrhages developed over the forehead, nose and upper chest. From this time on the patient failed to improve following transfusion. A grayish necrotic patch appeared on the right tonsil two weeks before death, and one week later there was evidence of bronchopneumonia. She lost strength rapidly, and on April 16, 1931, death occurred.

The gross findings at the autopsy performed by Doctor Charles L. Connor showed numerous varying-sized hemorrhages in all the serous coverings of the body cavities. The lymph nodes were but slightly enlarged and everywhere were firm and discrete. The liver was firm and slightly enlarged. It weighed 600 grams. The spleen was large and weighed 100 grams. Both kidneys were larger than normal and contained numerous minute pale green areas. The lungs showed no evidence of pneumonia, but there were many small subpleural hemorrhages. In the anterior cranial cavity beneath the dura on both sides lateral to the midline there were deposits of greenish material resembling old hemorrhage, and there were some recent bright hemorrhagic spots also present. The layers of the dura, particularly along the longitudinal sinus and around the lateral and straight sinuses were infiltrated with a greenish, cellular substance which appeared to be tumor. A small mass of similar material projected through the cribriform plate into the nasopharynx. The bone marrow in the upper third of the right femur appeared light red in color, cellular and seemed to contain very little fat.

On microscopic examination of the bone marrow, it was observed that there was an almost complete absence of fat, and that the normal architecture was in a large measure replaced by masses of cells. These cells contained large, clear, rounded nuclei with the chromatin clustered about the nuclear membrane, as seen in figure 3. The cells appeared immature and many contained an indented bay in the nucleus. None contained granules in the cytoplasm. This cell was considered a myeloblast rather than the so-called lymphoblast. Mitoses were frequently seen. There were very few polymorphonuclear leucocytes, but moderate numbers of myelocytes were discovered. Very small islands of erythroblastic tissue were seen, and rarely a megakaryocyte. Examination of the heart, lungs, liver, spleen, kidneys, adrenals, ovaries, and lymph nodes showed areas of infil-

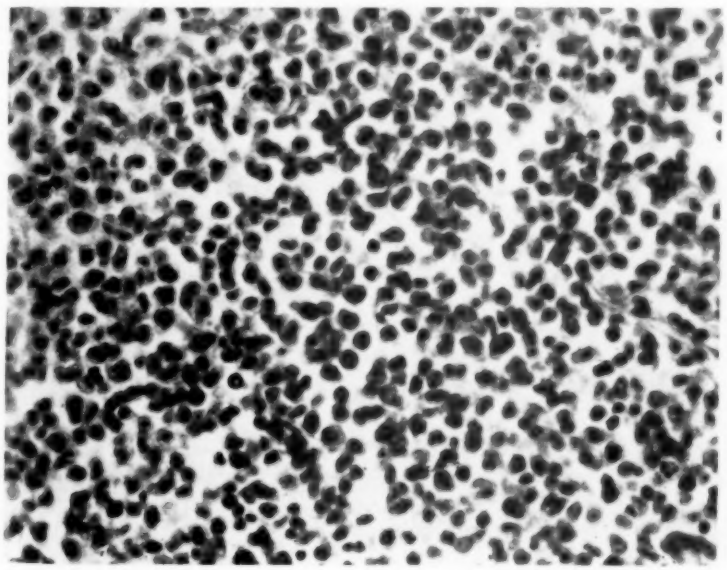

FIG. 3. Specimen of bone marrow removed from sternum of patient in case III. Note marked hyperplasia and presence of large numbers of immature leucocytes.

tration with cells resembling those described above. The tumor tissue removed from the dura was made up largely of this immature cell. It was believed that the concentration of the immature cells, as has been shown by Mallory, accounted for the pale green chloromatous color.

Comment

This, then, is another case of idiopathic neutropenia, the pathologic physiology of which apparently is entirely different from the two preceding cases. In contrast to cases I and II, there was in case IV increased cellularity of the bone marrow (figure 3) consisting almost entirely of leukoblastic tissue. Another patient, a female 56 years of age, presented a picture of the bone marrow similar to this in which active maturation of the leucocyte seemed retarded at the myeloblast stage.

Of rather rare occurrence is the development of severe leucopenia in conditions characterized by hemorrhagic tendencies, and in which abnormalities in platelet production appear fundamental. Minot[10] has reported such an instance in association with thrombocytopenic purpura hemorrhagica.

It is of course well known that severe leucopenia may also develop in association with certain abnormalities in red blood cell production. In patients with pernicious anemia, in relapse, leucopenia is more often present than absent. The occurrence of leucopenia in patients with sprue and Banti's disease are other examples. Two instances of leucopenia occurring in patients with severe anemia diagnosed as acquired hemolytic icterus may be briefly cited as follows:

Case V. An Italian male, 58 years of age, had been in good health prior to June, 1930, when he began to notice the gradual onset of a yellowish tinge in the whites of his eyes. In February, 1931, his skin appeared icteric and his sclerae were yellow in color. His hemoglobin was 40 per cent (S); the red blood cells numbered 2,130,000 per c. mm. and the white blood cells were 2,900 per c. mm. The blood platelets were slightly reduced in number, and 10 per cent of the nucleated cells in the stained blood smear were normoblasts. There was slightly increased hemolysis of the red blood cells to hypotonic salt solution. It is now one year after splenectomy and the patient appears in good health; he has a slight "secondary" anemia, but the leucocytes are present in normal numbers.

The illness from which the second patient suffered is not so clearly defined.

Case VI. This patient was a white male, 72 years of age, who had noticed increasing pallor and weakness of 3½ years' duration. During the past year his family physician had given him several transfusions of blood. When he entered the hospital, slight icterus of the sclerae was noted, and the spleen was moderately enlarged. His hemoglobin was 26 per cent (S); there were 1,160,000 red blood cells per c. mm., and the leucocytes were 2,300 per c. mm. The platelets were slightly reduced. The icterus index was 15. Reticulocyte counts made daily showed the presence of from 6 to 10 per cent of these cells. Analysis of the gastric content showed the presence of free hydrochloric acid. A biopsy of the sternal marrow was performed and the specimen of tissue removed was extremely cellular and made up almost entirely of normoblasts (figure 4). Because of the foregoing data and the failure to attribute the anemia to blood loss, pernicious anemia or tumor, acquired hemolytic icterus was considered the most likely diagnosis. Splenectomy was resorted to as a therapeutic agent. Two days after the operation the patient died following paralytic ileus. The report from the pathology laboratory was: splenomegaly, "type compatible with hemolytic icterus". A postmortem examination revealed the presence of marked erythro-

blastic and normoblastic hyperplasia of the bone marrow, but otherwise was essentially negative.

These cases, then, illustrate different types of neutropenia of obscure origin and represent different types of bone marrow reaction leading to alteration in leucopoiesis.

Benign Leucopenia of Obscure Origin

In group V of table I have been placed the number of patients in whom leucopenia was reported present but in whose records either no diagnosis appears or one that may be considered functional in nature. This group comprised 114 of the cases of leucopenia, or 9.7 per cent of the total. In this group appear the patients whose complaints were those of chronic fatigue, lassitude, lack of appetite, and vague sorts of distress of one sort or another. Among such cases some of the diagnoses were listed as neurasthenia, psychosis, hysteria and the various neuroses. Reference to similar cases have been made by Cabot,[11] Clough,[12] and Roberts and Kracke[2] who speak of them as states of "debility" associated with leucopenia. Disturbances in endocrine function[13] and a constitutional factor[14] have also been pointed out as having some possible relationship to decreased leucocyte formation. In this latter group the cause of the leucopenia must be considered intrinsic in character and decidedly obscure in origin.

Summary and Conclusions

1. Five cases of severe leucopenia of obscure origin are presented. Attention is called to the different types of bone marrow reaction occurring in the various cases; namely, aplasia of the bone marrow; depression of leucopoiesis only; hyperplasia of the leuko-

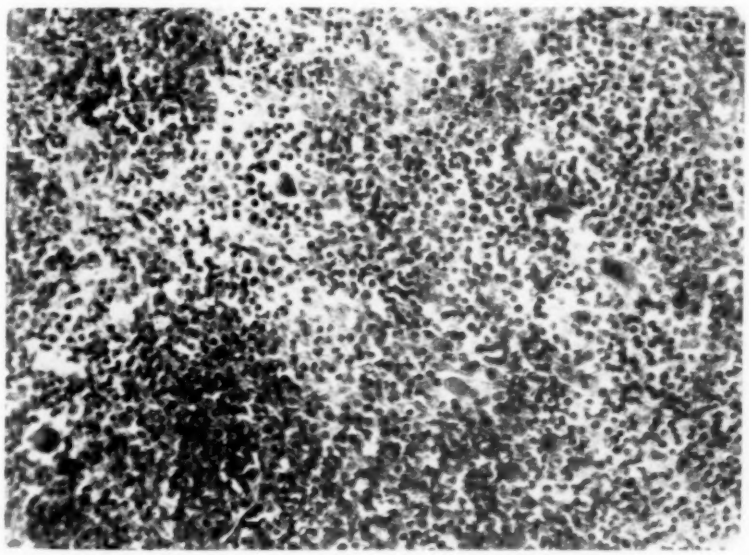

Fig. 4. Specimen of bone marrow removed at biopsy from sternum of patient in case VI. Note marked normoblastic hyperplasia.

poietic tissue; and hyperplasia of the erythropoietic tissue.

2. A case of leucopenia associated with lymphangitis of the arm in an adult female is reported in which recovery occurred during the course of administration of nucleotide K-96.

3. Among the 10,000 case records of patients cared for in the University of California Hospital between 1920 and 1931, inclusive, examination of the blood revealed leucopenia in 1,167 or 11.67 per cent of the cases.

4. 611 of the 10,000, or 52.4 per cent of the cases of leucopenia, occurred in females and 556, or 47.6 per cent, occurred in males. Thus, leucopenia was slightly more prevalent in females than males.

5. Leucopenia occurred frequently as a mild manifestation in patients with vague symptoms of one sort or another, such as chronic fatigue; 9.7 per cent of the cases of leucopenia were classified, therefore, as benign leucopenia of obscure origin.

6. A table of the frequency incidence of leucopenia is given.

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A Clinical Study of the Graves' Constitution and Its Relation to Thyroid Disease

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IT is not the purpose of this paper to discuss the relative merits of existing conceptions of thyroid disease, nor to add to such theories; but to present certain data—gathered and interpreted by the clinician—bearing on the constitutional background of hyperthyroidism as expounded by Warthin. From time to time mention has been made of the frequent association between thymic enlargement and thyroid disease, but Warthin's address entitled "The Constitutional Entity of Exophthalmic Goiter and So-Called Toxic Adenoma"[1] is the most comprehensive statement of the significance of this association and has given rise to the phrase "Graves' Constitution (Warthin)" which has been used by other writers to designate this concept. It would be out of place to review that address in this paper, but a brief statement of the essential features is necessary for clarity.

The clinical syndromes, variously spoken of as hyperthyroidism, toxic goiter, toxic adenoma, Graves' disease, and exophthalmic goiter, are well known to physicians generally. Since the time of Parry, Graves and von Basedow, the original triad of goiter, exophthalmos and tachycardia has been expanded by the addition of symptoms and signs referable to practically every organ in the body. Recent investigations have cast doubt on the assumption that thyroid dysfunction is the primary factor in this condition. The very multiplicity of names which has grown up to designate variations from the typical picture bears testimony to the complexity of the present conception and the difficulty of classifying cases seen. Warthin contends that there is, however, one underlying factor common to all who have this disease syndrome; and that factor is a constitutional abnormality, to which he has applied the term *Graves' constitution.*

The general appearance of the individual with this symptom complex is often so striking that the condition is recognized at a glance by even a relatively inexperienced observer. Quoting from Warthin[1] it is "expressed in *juvenile morphology* and rapid functional reaction". The essential anatomic stigmata, as seen at the autopsy table, are perhaps less widely recognized. Grossly there is found a persistent hyperplastic thymus. The importance and constancy of this finding was emphasized by Potter[2] in a review of twenty-two autopsies on cases of

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exophthalmic goiter, and more recently by Moschcowitz,[3] who, while not finding it in all instances, reports it in ninety-five per cent of his fatal cases. Of equal importance is a generalized hyperplasia of the lymphoid tissue throughout the body, including not only the lymph nodes but also Peyer's patches in the intestine and the minute islands of lymphoid tissue which are found scattered throughout the body. Scarcely less striking is the underdevelopment of the vascular system, particularly the heart and aorta. Likewise the hypoplasia of the adrenals, especially of the medullary portion, is of diagnostic and perhaps also of functional significance.

The lymphoid hyperplasia is the anatomical feature of diagnostic significance in the microscopic examination of the excised thyroid gland. The normal thyroid shows no lymphoid follicles, but there are scattered through it primitive lymph nodes, perhaps represented by only a few lymphoid cells, and so small as to be difficult of recognition. In the Graves' constitution these primitive nodes become hyperplastic, with the development of germinal centers. While this has been recognized by many writers, few have laid stress upon it, but Warthin[1, 4] has amply demonstrated its diagnostic significance as indicating Graves' constitution. He maintains that every case of exophthalmic goiter, hyperthyroidism, toxic goiter, toxic adenoma, or other variation of the clinical syndrome will show in the excised thyroid gland this evidence of a constitutional abnormality. He does not hold, however, that every person with Graves' constitution will show this clinical syndrome. While the individual with this constitutional abnormality is always potentially a subject for so-called thyroid disease, the condition may be dormant throughout his lifetime. We do not know what influences bring out the clinical syndrome. Consequently a simple goiter, a simple adenoma, an otherwise apparently normal thyroid, or even a thyroid of below normal function, may or may not belong to the Graves' constitution. An outline intended to clarify this relationship is given below in table I.

TABLE I

GRAVES' CONSTITUTION

(Lymphoid hyperplasia in thyroid)

Definite thyroid disease
- (a) Exophthalmic goiter
- (b) Toxic goiter, hyperthyroidism and other less well defined abnormalities
- (c) Toxic adenoma

Thyroid function normal or decreased

(Thyroid disease always potentially present, however)
- (a) Normal size and otherwise structurally normal thyroid
- (b) Diffuse colloid goiter.
- (c) Adenomatous goiter without toxicity

NO EVIDENCE OF GRAVES' CONSTITUTION

(Thyroid function normal or reduced)
- (a) Normal thyroids.
- (b) Diffuse colloid goiter
- (c) Adenomatous goiter.

This constitutional relationship to thyroid disease has been discussed at length in three papers appearing since Warthin's address. Simpson,[5] analyzing the cases at the Miami Valley Hospital corroborates Warthin's findings in their entirety. Hellwig[6] in a discussion based on fifty-four excised glands and six autopsies disagrees throughout with Warthin's conception. Quite aside from the meager extent of his

material, he has completely misinterpreted Warthin's idea of the Graves' constitution. He implies that since he found lymphocytic hyperplasia in 38.5 per cent of the cases showing no hyperthyroid symptoms there can be nothing diagnostic in this finding. As already pointed out, Warthin contends that Graves' constitution may be present in an otherwise normal thyroid, and that if the stimulus, concerning which we admittedly know little, is not present to set off the metabolic disturbance, the hyperthyroid symptoms may remain latent throughout the individual's lifetime.

A very interesting hypothesis has been advanced by Moschcowitz.[3] As already mentioned, he notes an almost uniform association of the thymico-lymphatic constitution with exophthalmic goiter. He maintains, however, that the constitutional background is a neuro-psychiatric instability, which he holds is most often seen in individuals of the thymico-lymphatic habitus, or to use Warthin's nomenclature, the Graves' constitution. He thus believes that there is an indirect relationship between the Graves' constitution and exophthalmic goiter, differing from Warthin, who believes that the neuro-psychiatric instability is merely an attribute of the constitution, and that the constitution is the fundamental requisite for thyroid disease.

In view of the conflicting ideas, I have attempted an evaluation of the importance of the Graves' constitution, approaching the problem as a clinician. In order to limit the amount of material, the period 1927 to 1930 was selected and all the cases were included which, during that period, had been studied on the medical service of the University of Michigan Hospital and subsequently transferred to the surgical service for thyroidectomy. The excised glands were all examined in the Department of Pathology of the University of Michigan, of which Dr. Warthin was at that time the director. The clinical records were thoroughly studied, including laboratory data, such as determinations of basal metabolic rate, and the case was evaluated clinically before any reference was made to the pathologist's report. The clinical and pathological findings were then tabulated and compared. A series of 245 cases was studied and the results are presented in table II. For the sake of clarity, I have avoided fine clinical differentiations, placing together in one group those conditions referred to as hyperthyroidism, exophthalmic goiter without eye signs, toxic goiter, etc.

Discussion

It will be seen at once that 90 per cent of the cases fall into Warthin's classification in just the manner which would be expected. The other 10 per cent in which there is an apparent disagreement between clinical findings and the pathological diagnosis calls for further study. I shall refrain as far as possible from theoretical conclusions, since a presentation of the facts concerning individual cases seems more to the point. For the sake of brevity the cases have been grouped in the above table and numbered with Roman numerals and these numbers will be used to identify them in the following discussion.

The four cases in group I, which clinically were typical exophthalmic

TABLE II

CLINICAL DIAGNOSIS	PATHOLOGICAL DIAGNOSIS			PERCENTAGE AGREEMENT
Group I	Exophthalmic goiter	Exophthalmic goiter with adenomas	No evidence of Graves' constitution	
Exophthalmic goiter with eye signs 67 cases	58 cases	5 cases	4 cases	93.9%
Group II Exophthalmic goiter without eye signs, hyperthyroidism, etc.	Exophthalmic goiter, or Graves' constitution			
71 cases	53 cases	14 cases	4 cases	94.4%
Group III Toxic adenoma 3 cases	3 cases			100%
Total 141 cases	114 cases	19 cases	8 cases	94.3%
Group IV Toxic adenoma 66 cases	Adenomatous goiter with Graves' constitution		No evidence of Graves' constitution	
	48 cases		18 cases	72.7%
Group V Non-toxic adenoma 38 cases	12 cases		26 cases	100%
	Percentage of non-toxic adenoma showing no evidence of Graves' constitution 68.4%			
Total cases 104	Agreement 86 cases		Disagreement 18 cases	82.7%
Grand Total 245 cases	Agreement 219 cases		Disagreement 26 cases	89.3%

goiter and pathologically showed no evidence of Graves' constitution, are perhaps the most significant. One of these four cases was known to have taken iodine for at least two months previous to operation and another stated that he had taken two or three kinds of goiter medicine before admission. In both these instances the pathologist stated that the microscopic appearance of the thyroid was that usually associated with excess use of iodine. The opinion has frequently been advanced that overuse of iodine may induce toxicity in an otherwise normal thyroid, an assertion which it is not within the scope of this paper to defend or contest. It was practically impossible to form any opinion concerning the rôle of iodine before admission in the cases reviewed in this study. The prevalence of iodine-containing nostrums posing as "goiter cures" and the frequency with which the patient has no idea of the character of medicine given him by his physi-

cians renders a clinical history of the amount of iodine taken extremely unreliable. While I make no attempt to explain the discrepancy in these two cases by the history of use of iodine, the possibility exists that it is a factor.

A third case not showing the histological criteria of Graves' constitution is in some respects not entirely typical of exophthalmic goiter. There was a history of 35 lbs. weight loss with a good appetite. Physical examination showed a warm, moist skin and marked exophthalmos. On the other hand, the heart rate was only 65 and the basal metabolism was variable, down to plus 21 per cent at one determination and up to plus 38 per cent four days later. Eight determinations were made showing this type of fluctuation and there was no drop in the basal rate following the use of Lugol's solution. While it seemed that this case must be included in the group of exophthalmic goiters, the diagnosis might be questioned by some. In the fourth case, however, there seems to be no question of the clinical diagnosis, the case being typical throughout of exophthalmic goiter, and the pathological examination of an adequate amount of material showed nothing indicating Graves' constitution.

In group II the diagnosis was open to dispute in one case listed as exophthalmic goiter without exophthalmos because of the presence of diabetes mellitus. The symptoms were those of the diabetes and the diagnosis of hyperthyroidism was based largely on a basal metabolic rate of plus 33 per cent dropping to plus 15 per cent after the use of Lugol's solution. In a second case similarly classified the outstanding features were 17 pounds weight loss with an appetite described as only fair, a pulse of 100, and a basal metabolic rate of plus 28 per cent dropping to plus 18 per cent on bed rest alone. While the picture suggests a so-called "mild hyperthyroidism" the array of clinical data is not entirely convincing. A third case is similar to this, weight loss of 20 pounds, fatigue, pulse 92, and a basal metabolic rate of plus 23 per cent dropping to 8 per cent without medication. The fourth case of non-agreement between clinical picture and the pathological criteria of Graves' constitution is quite typical of "exophthalmic goiter without exophthalmos", but the patient was 4 to 5 months pregnant. Whether this complicating factor disturbed the general picture is difficult to determine.

From this further study of these eight cases of discrepancy it will be seen that in one instance there is an apparent sharp departure from Warthin's conception of "thyroid disease" and the Graves' constitution. In the other seven cases the degree of divergence from this conception is more or less striking. While there is no attempt in this paper to explain away discrepancies and reconcile conflicting data, one other fact should be presented for the sake of fair consideration of the data. While several blocks were selected from each thyroid for microscopic examination, serial sections were not run. It has been demonstrated that in Graves' constitution the distribution of the lymphoid tissue is not uniform. It is entirely possible that some thyroids reported as not belonging to Graves' constitution may have contained lymphoid tissue which

was not present in the sections examined. Every clinician is familiar with the case of cancer or tuberculosis which is not diagnosed on biopsy because the diagnostic tissue was not present in what was excised for examination, and it is possible that Graves' constitution was not found in some of these cases because of an analogous situation.

In the group of the adenomatous goiters (group IV in table II) there are 18 cases which clinically would be considered "toxic adenoma", but in which the pathologist reported "no evidence of Graves' constitution". In this group evaluation of the data is more difficult, both from the clinical and the pathological points of view. As is well known, the clinical syndromes in this group are less well defined than in the case of "exophthalmic goiter"; and it is sometimes difficult to say whether a case should be classified as "simple adenoma" or "toxic adenoma". On the other hand, the pathologist is handicapped because the excised material often consists almost entirely of adenoma, and frequently an adenoma shows no evidence of Graves' constitution whereas the surrounding thyroid tissue shows the stigmata. Thus one of the 18 cases, clinically toxic and pathologically not of Graves' constitution, showed practically nothing in the excised tissue except a very large adenoma. It would be impossible to state what might have been found in the thyroid tissue very properly left behind or in that surrounding the adenoma, which had undergone a complete pressure atrophy.

The effect of congestive heart failure in confusing the clinical appearance of the case of adenomatous goiter is also generally recognized. Five cases were characterized by heart failure which dominated the clinical picture. The basal metabolic rate was definitely elevated in all these instances, but the diagnosis was not as clear-cut as might be desired.

Two other instances are worthy of special mention. One patient had diabetes mellitus. The basal rate was moderately elevated, plus 28 per cent on two occasions falling to plus 15 per cent before operation. The second case record contains a note to the effect that while the basal metabolic rate was definitely elevated, the patient at no time appeared toxic, nor did he have the classic physical signs of "toxic adenoma". None of these cases showed the pathological signs of Graves' constitution.

Regardless of whether the clinical diagnosis is discounted in the seven cases and the pathological opinion in the eighth there still remain ten cases in which it seems that no clinical diagnosis except "toxic adenoma" is possible, in which the excised material was adequate for microscopic examination and in which the pathological diagnosis was "no evidence of Graves' constitution". In group V, the non-toxic adenoma, as already explained, there are no discrepancies to be discussed. Those belonging to Graves' constitution are considered as potentially toxic, but may not have developed any toxic symptoms.

It has become proverbial that statistics can be made to prove or disprove almost any conclusion. Too often the writer approaches his problem with a

preconceived idea of what he wants to prove and naturally he is attracted by facts which appear to substantiate his views. Because of the fact that the very mass of material would make impossible individual consideration of cases, I have made no attempt to gather an imposing array of material. In order that clinical judgment should be uninfluenced by pathological findings, I have utilized the simple device of forming my clinical impression before reading the pathologist's report. I have not disregarded the recorded clinical diagnosis, but because of the fact that it is recorded *after* reading the pathologist's report and accordingly is probably influenced by that report, I have also considered all the other clinical data such as history, physical examination and ward notes. Finally in those instances where the diagnosis seemed open to question, I have given the salient features of the case record. It is my hope that this clinically interpreted data will be of more value than a simple comparison of recorded diagnoses. Using this approach it is apparent that in 245 cases of thyroid disease studied, 89.4 per cent of the clinical diagnoses were in agreement with Warthin's conception of the Graves' constitution as a fundamental factor in these disturbances, the pathological examination of the excised thyroid gland being the criterion of the existence or non-existence of the constitution. In the remaining 10 per cent the clinical diagnosis may be considered open to question in certain instances, but on the basis of the information available it must be said that these cases do not substantiate Warthin's premise.

Conclusions

It is not within the scope of this paper to explain why the comparison of clinical and pathological findings does not reach 100 per cent of agreement. I have suggested certain possibilities which may explain some instances of discrepancy, but these are impossible of proof with data at hand. I do not wish to be either defendant of, or apologist for, the view presented by Warthin. However, the occurrence of a specific constitutional type in nine out of ten instances of this metabolic disturbance cannot be without significance. I do not feel that my statistics establish beyond question that Graves' constitution is necessary to the development of exophthalmic goiter or the so-called toxic adenoma. They do, however, indicate that these conditions usually develop in the individual with this constitutional anomaly. It has not been my purpose to emphasize a new diagnostic criterion for the pathologist. The conception of the Graves' constitution as presented by Warthin is far more than that. It is, in fact, fundamental in the pathogenesis of thyroid disease and has bearing on the rationale of treatment. My findings, in the main, support Warthin's view, and it is my hope that there may be studies from other sources which will further clarify the situation, either by addition of further support or by refutation of this conception.

Summary

1. Graves' constitution was described by Warthin and others as a congenital body type always present in the clinical syndromes of Graves' dis-

ease, hyperthyroidism, and toxic adenoma.

2. A group of cases, from which the thyroid gland was pathologically examined following operation, has been clinically interpreted and studied.

3. Of 245 cases thus studied 219, or 89.4 per cent, were in clinical agreement with Warthin's conception. In 141 cases of exophthalmic goiter, the agreement was 94.3 per cent; in 104 cases of adenomatous goiter, the agreement was 82.7 per cent.

4. In view of these findings, Warthin's conception of the Graves' constitution appears as an important contribution toward a more complete understanding of thyroid disease. The initiating factor of the thyrotoxic symptoms is not clear and many phases of the subject are still obscure; but it seems evident that a constitutional anomaly, present from birth, is a factor of great importance.

I wish to acknowledge my great indebtedness to the late Dr. A. S. Warthin for stimulation to undertake this problem, and for encouragement to carry it through to the end. I also wish to give recognition to Dr. C. V. Weller, Professor of Pathology and Director of the Pathological Laboratories of the University of Michigan, for his assistance in the evaluation of the pathological material in the cases used as a basis for this report.

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Photosensitization

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There are phenomena in a considerable number which are produced in living systems by substances not normally present in these systems which sensitize them to light. These phenomena are described collectively under the term *photodynamic action;* they are of widespread occurrence and manifest themselves in various ways. As examples may be cited: the hemolysis of red cells and the destruction of bacteria by light and eosin, and the poisoning of domestic animals by substances ingested from buckwheat. As has been pointed out by Blum (1932), these phenomena are apparently based upon similar chemical reactions, since, so far as they have been studied, all require the presence of molecular oxygen. This separates them at once from a number of similar phenomena produced by ultraviolet light without sensitizers, which take place in either the presence or absence of oxygen. It will be the purpose of the present communication to consider the possible relationship of such mechanisms to clinical medicine.

We will consider first the relationship of such mechanisms to certain disease entities, known principally to the dermatologist, which may be classed under the term "light sensitivity". Diseases falling under this head which have been suggested as due to photodynamic sensitization are *Hydroa aestivale seu vacciniforme, Xeroderma pigmentosum, Eczema solare,* and others. *Hydroa,* at least, has been widely accepted as a photodynamic phenomenon in which *hematoporphyrin* acts as the sensitizer. I shall not attempt to discuss any of these diseases from a symptomatic standpoint, but only to consider the possibility of abnormal photosensitizers as etiological factors in such conditions.

Before proceeding further, it will be useful to consider a few fundamental principles of photochemistry and of the physiological action of light. Any primary photochemical reaction is assumed to follow the Stark-Einstein equivalence law, according to which a molecule absorbs a quantum of light energy and becomes an activated molecule which persists in the activated state for an extremely short time. This may be represented by the equation

$$S + h\nu = S'$$

Where S is the light-absorbing molecule, $h\nu$ the light quantum and S′ the activated molecule. The molecule S can only absorb light of certain

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wave lengths so that only specific wave lengths can activate it. During the short period of activation the molecule may react chemically with other molecules, or undergo other fates which need not concern us here. If a chemical reaction takes place, the type of reaction which occurs will depend not only upon the kind of activated molecule but upon the kind and number of other molecules in the system with which the activated molecule may come in contact. Thus the reaction which takes place depends not only upon the photochemically active molecule and the light which it absorbs, but also upon the other components of the reacting system.

In the human organism there are present certain mechanisms which are stimulated by light. We may assume that the light is absorbed by certain photoactive substances which initiate these reactions, and thus the reactions are produced only by light of definite wave lengths which are absorbed by this substance. The activating radiations must all lie within the absorption spectrum of the photoactive substance, although all the wave lengths absorbed need not produce the photochemical reaction. The mechanisms of this type which are definitely known in the normal human body are: (a) pigmentation of the skin, (b) erythema, and (c) the calcium-phosphorus balance. The wave lengths bringing about these reactions are all in the ultraviolet region, below about 350 mμ (see figure 1). These reactions may be quite complex in their nature; the calcium-phosphorus balance mechanism is probably due to chemical changes brought about in ergosterol or similar substances circulating in the blood, but the other mechanisms are not so simply explainable. Now it is possible that an upset at any point in one of these

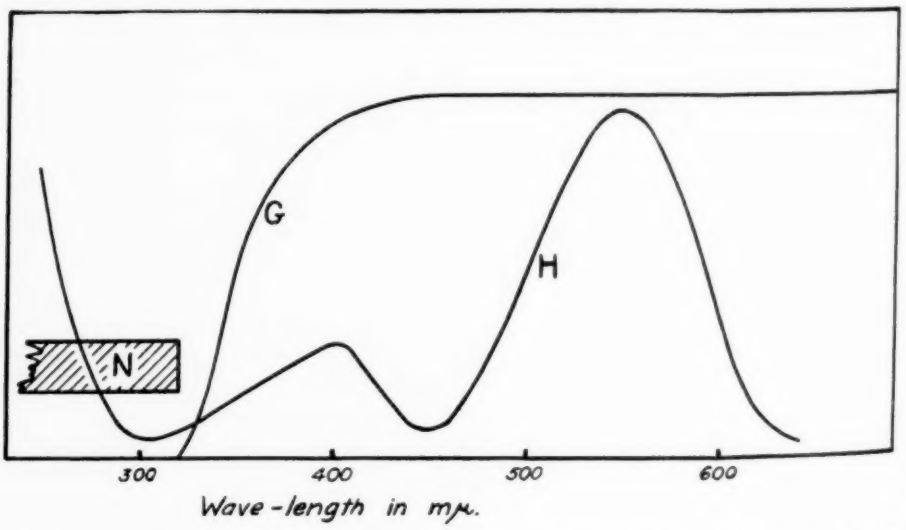

FIG. 1. H = approximate absorption curve of hematoporphyrin, showing position of absorption maxima at 400 mμ and 560 mμ; only the general regions of absorption are shown, actually the curve is much more complex. N = region of wave lengths producing normal skin reactions. G = lower limit of transmission of window glass.

mechanisms might result in a hypersensitivity of the organism to light, expressed in terms of that mechanism. Thus, for example, it may be that *Xeroderma pigmentosum* is due to an upset in some part of the pigment forming mechanism which does not involve the primary photochemical reaction in any way. In such case the light sensitivity would be brought about by the same rays which bring about the normal pigmentation reaction in the organism.

On the other hand, we have the possibility that light sensitivity may be brought about by abnormally present photoactive substances. Sensitization by such substances might be expected to bring about totally different reactions from those due to the photosensitive mechanisms normally extant in the body, although we cannot neglect the possibility that such abnormal photoactive substances might sensitize the normally existing mechanisms and thus exaggerate these reactions. In either case, the wave lengths bringing about these photochemical reactions would be specific for the abnormally present photoactive substance and must lie within the absorption spectrum of that substance. This should provide us with a possible means of distinguishing between the two alternative mechanisms for the light sensitivity mentioned above, on the basis of the wave lengths of light which are active in bringing about these responses, except in the event that the absorption spectrum of the abnormal sensitizer should correspond approximately with that of the photosensitive substances producing the normal light reactions. In other words, if we find that wave lengths other than those bringing about the normal reactions of the body to light (around 350 mμ), bring about reactions in the skin or elsewhere, we are probably justified in assuming the presence of an abnormal sensitizer.

Hydroa aestivale seu vacciniforme, a condition in which vacciniform lesions of the skin appear, usually occurs during the sunny period of the year, and is considered generally to be a condition of light sensitivity. Furthermore, the condition is quite generally stated to be due to the photosensitizing action of the abnormal blood pigment, *hematoporphyrin*. As a matter of fact, hematoporphyrin is not actually a naturally occurring pigment, but is a substance produced in the laboratory from hemoglobin. The naturally occurring pigments are uroporphyrin and stercoporphyrin (see Garrod, 1923) and possibly others, which, however, are very similar to hematoporphyrin in structure and properties; the term hematophorphyrin has been often used collectively to describe the naturally occurring porphyrins. It is interesting to find in the examination of the literature, that porphyrins are very frequently not demonstrable in the blood or urine of patients showing the lesions definitely associated with the diagnosis of Hydroa. This indicates that the porphyrins of this type are not always associated with the condition diagnosed as Hydroa, and it also appears doubtful if this particular type of skin lesion always appears as a result of exposure of the skin to the sun's rays. We find actually that some of the Hydroa patients in whom the development of the lesions has been quite

definitely associated with exposure to light have shown porphyrins in the blood or urine, while others have not (see Hausmann and Haxthausen, 1929; Barber *et al,* 1926).

Furthermore, an interesting situation appears when we consider the wave lengths active in bringing about skin lesions in Hydroa patients in the few cases in which this has been examined. The results of such examinations are not clearcut but in most cases the sensitivity to light is definitely in the ultraviolet region, with one or two possible exceptions in which there has been some sensitivity to visible radiation (see Hausmann and Haxthausen, 1929; and Barber *et al,* 1926). Now hematoporphyrin and the naturally occurring porphyrins show strong absorption in the visible region around 550 mμ (see figure 1), and animals sensitized by the injection of hematoporphyrin develop very striking symptoms, including skin lesions, when exposed to light of such wave lengths. The experimental animals in this case include man,* as Meyer-Betz (1913) performed the experiment upon himself; it should be noted, however, that although Meyer-Betz developed severe edema of the skin and definite localized skin destruction when exposed to strong irradiation, he did not develop any hydroa-like eruption. He was sensitive to radiations which had passed through window glass which would have been extremely weak in ultraviolet radiation. This experimental evidence has often been invoked to establish the relationship between hematoporphyrin and Hydroa, but the lack of correspondence between the radiations active in the two cases renders this evidence almost valueless. The naturally occurring porphyrins, uroporphyrin and stercoporphyrin, are very similar to hematoporphyrin in chemical structure and show practically the same absorption spectrum. Hausmann and Krumpel (1927) have shown that all these porphyrins show absorption in the violet and ultraviolet with a maximum at about 400 mμ (see figure 1), and moreover, Hausmann and Sonne (1927) and Lassen (1927) have demonstrated that photodynamic sensitization occurs in this region. Thus it is possible that hematoporphyrin may sensitize Hydroa patients in this region, but no explanation is offered by this assumption for the failure of these substances to sensitize the Hydroa patients to light of 550 mμ.

Fischer has suggested that the porphyrins themselves may not be the photosensitizers, but the porphyrinogens or leucobases of the porphyrins. The porphyrinogens absorb principally in the ultraviolet and thus their sensitizing action would be in this region; the absorption of these substances in the ultraviolet has been demonstrated by Hausmann and Krumpel (1929). Unfortunately, these wave lengths are in the same general region to which the normal skin mechanisms react, so that we cannot easily prove or refute this hypothesis by studying the wave lengths which produce Hydroa. The porphyrinogens are supposedly changed to porphyrins by the action of light, according to this hypothesis, so that we are still presented with the question as to why the porphyrins found in the blood stream do not produce sensitization in the visible region.

Another argument against the con-

cept that this disease is produced by a photoactive substance circulating in the blood is that in certain of the cases studied it was found that only those skin areas which had previously shown the Hydroa lesions could be sensitized by ultraviolet radiation. This would indicate that the reaction produced by this means represents a hyperactivity of the normal erythema reaction brought about by the ultraviolet wave lengths and is not due to an abnormal sensitizer circulating in the blood stream, since in the latter case all skin areas should be light sensitive to approximately the same extent. Furthermore, porphyrins are frequently found in the blood stream and in the urine in conditions not associated with light sensitivity. We may cite as examples, the condition following veronal or lead poisoning, often referred to as *hematoporphyria toxica,* and the idiopathic condition *hematoporphyria acuta* (see Rothman, 1926; and Mason and Farnham, 1931). In these conditions considerable quantities of porphyrin may be demonstrable in the blood and urine, but only rarely are these cases light sensitive (see Hausmann and Haxthausen, 1929).

The problem is obviously much more complicated than we are led to expect, and the exact relationship between porphyrins and Hydroa is certainly not clearly understood. It is quite possible that the porphyrins play no part whatsoever in the light sensitivity or, again, that they represent products of skin injury. The relation of abnormal sensitizers to other light sensitive diseases is still more obscure. Further well-controlled observations on light sensitive cases should prove of great value in settling this question. It would be of considerable value if observations could be made to determine whether or not individuals showing porphyrins in the blood or urine were actually light sensitive, and if so, whether to visible light as well as to ultraviolet. The latter fact should be determinable by exposing the subject to sunlight with a part of the skin exposed directly, and a part protected by window glass which cuts out practically all ultraviolet radiation active in bringing about the normal skin reactions (see figure 1).

Photosensitization by ingested substances which enter the blood stream occurs in domestic animals. At least two well established instances are the conditions of *fagopirismus and hypericismus* which develop when animals are fed upon buckwheat or St. Johnswort respectively. No examples of such sensitization by foods are known in man although the possibility exists. Buckwheat poisoning has been described (Smith, 1909) but this was undoubtedly allergy and not photosensitization.*

Various instances of photosensitization as the result of the therapeutic use of photoactive substances in the clinic have occurred. The substances have sometimes been given by mouth, sometimes by intravenous or subcutaneous injection and sometimes applied to the skin. The earliest example is that of Prime (Hausmann, 1923, p.

*The well-established opinions of the laity that "buckwheat rash" develops in the spring, and that buckwheat should not be eaten during the summer months are explainable with difficulty unless buckwheat has a photodynamic effect in man as well as in the lower animals. EDITOR.

156) who attempted to treat twenty-six epileptic patients with the bromine containing compound *eosin*. His patients developed a dermatitis and showed damage to the nails, particularly the thumbnail, which was most exposed to light. Jausion and Marceron (1925) observed sunstroke ("coup de soleil") in nine of twenty soldiers treated with *trypaflavine* for gonorrhea; dermatitis and excessive pigmentation were described by other observers using various *acridine* preparations (Hausmann and Haxthausen, 1929, p. 79-80). Numerous instances of sensitization by acridine compounds have been described for workers using this substance, or substances containing it, in technical procedures. The writer has recently been informed of a case in which *rose-bengale* had been used in liver function test, in which obstruction was present so that the dye was retained and the patient was photosensitive for a short time.

Dermatitis produced by substances applied to the skin have been described as photosensitizations (see Hausmann and Haxthausen, 1929), some of which may fall under this group. The toilet water or "Berlock" dermatitis which has been frequently described within the last few years is probably not a photodynamic effect.

It is probably safe to predict that more cases of photosensitization will soon be described, as the use of sensitizing substances in light therapy is being taken up to a certain extent. The use of photosensitizers (*erythrosin*) in light therapy was tried out in Finsen's Institute shortly after 1900 and subsequently abandoned. It was also tried out by Jesionek and Tappeiner (1905) in the treatment of superficial carcinoma with no definite results. Recently the use of sensitizers as a therapeutic measure has again been taken up. Gyorgi and Gottlieb (1923) claimed to have obtained good results in the treatment of rickets, and Macht and Anderson (1928) for the treatment of pernicious anemia using eosin as a sensitizer. Others have apparently applied the treatment to any condition which had at any time been treated by ultraviolet light; the sensitizers used include *trypaflavine*, and *methylene blue* as well as the fluorescein dyes such as eosin and erythrosin.

I do not wish to deny the results claimed by these workers, but only to point out certain dangers which present themselves from a more or less theoretical viewpoint. Sensitizers of the type used are all known to produce damage to living cells by oxidative processes involving molecular oxygen. Other photochemical reactions of the sensitizers may be produced in organic or inorganic systems, e.g., the sensitization of the photographic plate, but such have never been demonstrated in living tissues (see Blum, 1932). It seems, for instance, highly improbable, though not impossible, that such substances should sensitize the particular process involved in the treatment of rickets, viz., the transformation of ergosterol to vitamin D, and much more probable that the destructive oxidative effects would predominate. The former was apparently the thesis assumed by Strauch (1930) who injected hematoporphyrin into two farmer boys having rickets. Strauch observed an erythema in these children upon exposure to light and came to the con-

clusion that the treatment might be effective in curing rickets; he does not state, however, whether the patients recovered from rickets or not. I do not wish to deny that photochemotherapy may have some application, but such methods should not be applied to patients without more animal experimentation, where possible, to establish the results.

The assumption that visible light and a sensitizer will accomplish the same reactions as ultraviolet light is without theoretical or experimental support at the present time. Both accomplish the same gross effect, erythema. The histological effects on the skin are described as being the same by Levy (1929), but Videbech (1931) states that there is much more injury to connective tissue in the case of the photosensitized erythema; this may be a question of the extent of the irradiation, etc.

The dangers arising from the use of photosensitizers in therapeutics cannot be too strongly emphasized. If such methods are applied, they should at least be used with great caution. It should be remembered that Meyer-Betz (1913) remained sensitive to light for several months after a single injection of hematoporphyrin and that lasting damage can be done by the incautious use of such methods.

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The Contributions of Medicine

"IT HAS been inevitable that medical services should be influenced by the various economic and social changes which have developed in this country in recent years. While changes in industrial and community life are having an influence on the health of the people, the enormous growth of knowledge of disease and methods of control and prevention have revolutionized conditions of living during the last fifty years. The death rate at present is only about three-fifths of what it was a half century ago. The virtual elimination of smallpox, typhoid fever, yellow fever, typhus, bubonic plague, and cholera from large areas of the world, the rapid reduction in the incidence of tuberculosis and diphtheria, and the control of hookworm, malaria, and other parasitic diseases suggest a few of the striking contributions which science is making to the safety and comfort of modern life, contributions which in some instances have transformed living and working conditions in large sections of the country. Special attention to nutrition and the influence of foods, minerals, and vitamins on the health of the individual, and efforts to secure a better understanding of the mental processes, which is fundamental for a sound program of dealing with human behavior, are likely to result in further contributions.

"No difficulty is experienced in demonstrating that physical and mental health is the greatest asset of a nation as well as of an individual. It is one of the necessities of everyday life. The prosperity and happiness of a people are largely dependent upon mental and physical vigor. Ill health and its effects are recognized widely as one of the major causes of dependency and unemployment. The most pressing health problem is to devise a permanent and comprehensive program of conserving health and treating illness and disability which will become an essential part of the cooperative endeavor known as civilization."

(From the *Final Report of the Commission on Medical Education*, 1932; WILLARD C. RAPPLEYE, A.M., M.D., F.A.C.P., Director of Study. Pages 17-18.)

The Cardiac Complications of Trichterbrust

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TO an unusual thoracic deformity characterized by an oval or circular, almost funnel-shaped depression of the middle of the anterior thoracic wall, the deepest part of which lies in the sternum itself, the name *Trichterbrust,* the German for funnel-breast, has come into common use in many languages. Von Frühwald's definition includes a clause making specific mention of the diminution of the capacity of the thorax and Dachter included in his criteria, "Increasing depression of the sternum with the age of the patient and a progressive enlargement of the transverse diameter as the depression is deepened". In one of the earliest contributions to the subject, Eggel had pointed out this last-mentioned feature of the deformity, when he described "a compensation of the spatial defects, produced by the depression of the anterior chest-wall, which is accomplished in three ways: (1) the enlargement of the antero-posterior diameter in the mammillary lines, (2) the very significant enlargement of the transverse, and (3) the enlargement of the vertical diameter of the thorax; the latter fact must be concluded from the low position of the upper limit of hepatic dulness and the displacement of the cardiac apex to a deep position."

It is obvious that such a deformity may cause displacement of various organs and interference with their function. Here our attention will be confined chiefly to the anatomical and physiological effects of Trichterbrust upon the heart.

Historically, the credit for presenting the condition to the profession as a clinical entity and for the first use of the name now so generally employed, goes to Wilhelm Ebstein, who in 1882 summarized the reports of five cases in the literature, coördinated them as a single disease-picture and used the word "Trichterbrust" to describe the clinical entity. Prior to his publication another case had been reported to which Ebstein did not refer. This was the case of Williams, recorded in the "Transactions of the Pathological Society of London" for 1872. The patient in this instance was a "lad of 17" who "was born with this hollow in his chest".

In discussing the history of the subject practically all authors refer to the anonymous communication which appeared in the Gaz. des Hôp. in 1860 as the first description of funnel-breast. In the same year Woillez reported a case with a careful study. It seems likely that Woillez reported

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a patient who had been seen and discussed by Rokitansky in 1857, a medical student from a German University who was making the rounds of the medical schools of Europe about that time (E. von Ebstein). W. von Ebstein mentioned that the local Pathological Institute at Göttingen contained a plaster cast designated as demonstrating "congenital collapse of the sternum" which completely conforms to the deformity described. Prof. Orth was authority for the statement that the plaster model dated from 1850. An even more interesting note on the historical aspects of this subject was contributed by Erich von Ebstein in 1921, the author of an extensive article on Trichterbrust in 1909. In this brief reference the statement is made that attention had already been paid to these conditions by the end of the sixteenth century. A short, excellent observation occurs in the principal work of the Freiburg physician, Johann Schenck, of Graefenberg (1531-1598). He set for himself the difficult but very useful task of collecting the literature on a large scale. In order to make this possible he was not satisfied to take from works at hand and to add cases from his own large practice but he was in communication with the foremost correspondents of his time. He quotes Johann Bauhinus who described the principal clinical symptoms—"dyspnea, associated with cough increasing to paroxysms of suffocation". From this same Bauhinus is quoted a description of a case in which "The sternum with the ribs was turned inward from birth, causing difficulty of breathing. The patient was a boy of seven in whom the ensiform cartilage was turned toward the interior of the body so that a great cavity appeared". Doubtless the funnel-shaped breast described by Eggel in 1871 as "A Rare Deformity of the Thorax" has not actually been so uncommon as early writers presumed.

As to the anatomical characteristics of Trichterbrust, Wolostnich says there is practical agreement as to the following picture: "The upper limit of the Trichterbrust is formed by the connecting line between the manubrium and corpus sterni; from this situation the funnel-shaped depression runs downward and backward; in most instances the greatest depth is reached at the scrobiculus cordis. The rounded base has a very slight extension, the diameter of which is variable. From the base of this depression its wall runs forward in such a manner, corresponding to its funnel-shape, that on the anterior wall of the body the maximum breadth varies between 9 and 17.2 cm. The center of the depression is not always in the middle of the sternum and the line of depth of the furrow is not always straight." This circular or oval depression at the lower end of the sternum may reach a depth of several centimeters, as much as 6 or 7. Picqué and Colombani measured the capacity of the depression in cubic centimeters of water. In the less pronounced cases this amounted to about 50 c.c. but in the more severe to 170 c.c. or more.

As one result of this depression various degrees of cardiac displacement have been reported. Versé studied the thorax of a female subject who died at the age of 48 years. The

thorax was removed *in toto* and hardened for two days. The lower end of the corpus sterni included the deepest part of the depression and almost touched the spine at the level of the cartilage between the tenth and eleventh thoracic vertebrae. Here the distance from bone to bone measured only about 1 cm. This could be increased to 1½ cm. by lifting the sternum. The thin cartilaginous processus xiphoides was 4 cm. long and directed obliquely forward; its tip was distant from the spine 3.7 cm. The chief mass of the heart was found to the left of the midline. Almost the entire left ventricle and a small part of the left auricle with the greatest section of the mitral valve were found lateral to the left parasternal line. Von Bien reported an autopsy at which the heart was found to lie "entirely in the left half of the thorax, while the right half was filled by the lungs; behind the heart a thin half-moon-shaped section of the lung was seen. The heart in its entirety was displaced to the left. If one drew the median line of the body in such a way that the line of the ensiform process was connected with the most ventrally situated points of the vertebrae it so happened that not a single section of the heart lay in the right half of the body. But corresponding to the displacement of the sternum to the left a part of the heart was in contact with the inner surface of the sternum, a small portion of the anterior wall of the right ventricle and a small part of the right auricle attached thereto ... If, at the place of deepest depression, one lifted the anterior wall from the heart a deep depression of the auricle was seen which extended to a portion of the right ventricle." In this case the displacement involved the roots of the vessels at the base of the heart. At the time of his report in 1920, Stadtmüller stated that he could find in the literature only eight reports of autopsies; in four of these the subjects were adults. He added the report of an autopsy upon the body of a man of 60 and stated that the heart showed (1) total displacement to the left and (2) the appearance of being turned about its sagittal axis. Von Hoffmeister quotes Henschen and Nägeli as having observed a significant pressure point on the right ventricle. Rudolph von Pohl has described another type of cardiac involvement in those cases of Trichterbrust in which the median position of the heart is retained: "The thoracic deformity produces an indentation of the heart in front, corresponding to the in-bowing of the anterior thoracic wall, and the anteroposterior cardiac diameter is diminished."

Clinically, displacement has frequently been noted. In recent years roentgenological examination has confirmed this finding. Sauerbruch stated that "by physical examination and the roentgen-ray one may determine displacement of the heart to the left with or without simultaneous rotation about its axis". L. Meyer, von Hoffmeister and Alexander all wrote of the demonstration of displacement to the left by means of the roentgenological examination. Von Rösler, discussing the results of examination by the X-ray in cases of thoracic deformity, remarked regarding Trichterbrust: "It is plausible that in high-grade cases,

through the flattening of the heart the cardiac work is unfavorably influenced, the normal systolic-diastolic change of form and rotation must be made difficult, the circulatory relations of the blood in the heart itself, probably also the position and form of the venous openings, may be changed."

In spite of the marked deformity, the changes in the dimensions of the space normally occupied by the heart and the anatomical evidence of change in the position and even of the shape of the heart, those who have contributed to our knowledge of the subject are not agreed as to the effect of the deformity upon cardiac function. Von Eggel's patient, in whom the distance from the deepest part of the sternum to the corresponding vertebral spine was only 11 cm. (according to Vierordt the normal distance from the ensiform to the thoracic spine is 15 to 19 cm.), "could not lift such heavy burdens nor run as fast as others of like occupation, but without distress he carried on his work as an efficient farmer, walked with firm tread and showed no trace of dyspnea, to say nothing of cyanosis. When he was six years old his physician had predicted that he would not outlive his twentieth year. Within four weeks of his birth the breast was so sunken that an egg could have been laid in the furrow". In von Flesch's case, although the depression was extreme, "respiratory pains had never been present; even hard work can be done without dyspnea". Graeffner made a similar observation. In 1911, Groedel reviewed his records for cases of Trichterbrust and reported three well-marked instances. It was his opinion that satisfactory evidence was not at hand to warrant the assertion that this deformity is responsible for cardiac failure. He contends that while Trichterbrust does change the form and shape of the thorax, it does not change the content. The lung accommodates itself to displacement as does the heart, without necessarily involving these organs in functional damage. Groedel raised a question of interest and importance in the determination of the relationship of symptoms to the deformity. He emphasized the frequent association of Trichterbrust with the habitus asthenicus, in which condition are often found symptoms of circulatory embarrassment similar to those described as resulting from the displacement or pressure produced by Trichterbrust. In the latter condition surgical procedures to relieve dyspnea or other disturbances attributable to impairment of cardiac function must be based upon a conviction of the relationship between the deformity and the symptoms. The frequency of associated stigmata of the habitus asthenicus calls for careful consideration as to the amount of permanent relief which may be expected by surgical treatment of the deformity. In this connection we may quote again from Wolostnich who reviewed the literature thirty years after the first publication of von Ebstein: "The function of the heart and the pulmonary capacity commonly remain normal. The affected individuals have no pains from their Trichterbrust and very often—as is definitely stated in many works—the whole deformity presents an accidental and incidental finding upon the examination of a patient who has sought the

physician for other reasons." Kuhns has recently expressed this conservative statement: "With careful pathological studies and fuller understanding of the physiological disturbances which such displacement of thoracic and abdominal viscera produces, has come an appreciation of the rôle of this condition in inducing fatigue, subnormal health and disease."

While in general these views of the lack of demonstrable connection between the deformity and cardiac or respiratory symptoms have been dominant since the condition was first described, attempts have been made, first by orthopedic procedures and later by surgery, to correct the deformity and thereby relieve associated symptoms attributed by the operators to the deformity. In 1911, Ludwig Meyer performed the first operation for such relief. He prefaces the description of the technic with a discussion of the case and remarks that "The literature tells us little or nothing of the symptoms which result from the deformity ... For a patient of this sort, when he suffers from dyspnea, therapy can only be effective when it changes the anatomical conditions fundamentally and provides conditions compatible with respiration." The operation consisted in the removal of the second and third costal cartilages of the right side, each about 2½ cm. in length. Von Hoffmeister, reporting a case from Lexer's clinic in 1927, implied that the result in Meyer's case was not satisfactory. After describing resection of a considerable portion of the sternum in a young man whose symptoms were dyspnea upon exertion, sticking pain in the region of the heart and palpitation, he makes this remark: "That only an extensive removal of the diseased portion gives a result, the unsuccessful attempt of L. Meyer has shown." Sauerbruch reported a successful operation upon a young man of 18 years with congenital Trichterbrust, whose symptoms were cardiac irregularity and dyspnea upon exertion. The operation was undertaken because "the patient was not able to do his work in his father's watch factory, since the least effort caused palpitation and a feeling of oppression". After some two or three weeks in the hospital, prior to operation, a short walk on a street with a moderate rise produced "marked cardiac irregularity and dyspnea" which were attributed to a mechanical interference with cardiac function. It was the surgeon's idea that "removal of the rigid funnel would give more room to the heart and free it from the constricting pressure of the thoracic wall". On the left side the costal cartilages with portions of the sixth to the ninth ribs (the length of each resected portion was about 3 cm.) and about one-half of the sternum corresponding, were removed. The post-operative course was smooth. Three years later the patient had gained weight, felt well and was working twelve to fourteen hours a day. Von Hoffmeister reported from Lexer's clinic the case of a young man of 19, who had complained for two years of cardiac pain, dyspnea upon exertion and palpitation. Below the attachment of the fifth rib the sternum with the costal cartilages was removed. Twelve weeks after operation the general condition was essentially improved, there was a gain in weight and dyspnea

was present in only slight degree . The pains in the heart were definitely less in comparison to those earlier observed. Zahradnicek reported the case of a boy of 16 with a high degree of funnel-shaped chest. The sagittal diameter at the point of depression was about 10 cm. The patient was dyspneic and had palpitation. The operation consisted in perforation of the sternum and the introduction of two wires which were used for traction. The result was quite satisfactory. Two cases of "traumatic pectus excavatum" were reported by Alexander in 1931. A boy of 16, whose depression had followed an injury while wrestling, complained of dyspnea and occasional dysphagia ... Ten months after operation the patient wrote that he had no pain nor dyspnea even upon exertion, and that the correction of the deformity was maintained. The second patient was a woman of 20 whose deformity followed an automobile accident. She complained of severe pain in the region of the heart, of dyspnea and palpitation. The pain was usually referred to the left shoulder. The cardiac pain was disabling and unrelieved by long rest. She had no cardiac, shoulder or left axillary pain after the operation.

These few cases serve to confirm Sauerbruch's opinion that "high-grade disturbance of cardiac and pulmonary function with signs of congestion in the peripheral vessels may occur". Proper selection of cases justifies surgical interference in certain cases of Trichterbrust. Two important principles should govern the decision as to operation in any given case: (1) Trichterbrust is not in itself an indication for operation; (2) there should be a high probability of relationship between the symptoms and the deformity before operation is justifiable. An interesting sidelight on the conditions proposed is derived from Gerstenberg's monograph published in 1904. He compiled a list of twenty-one published cases in which the measurements of the deformity had been given. The oldest patient in this group was 39 years of age. One may conclude that the condition is sufficiently disabling to bring its victims to the attention of the physician in early life. This fact alone should stimulate us to continued effort in our search for a means of relieving the deformity which forebodes only increasing disability and shortening of life. To experienced and careful surgeons, especially to those skillful in thoracic work, the indications for surgery just mentioned may reasonably be liberalized in the presence of individual problems.

Case Reports

In the past year two cases of Trichterbrust with cardiac symptoms have come under our observation. The *first* patient was a young woman of 19, unmarried. She complained of rapidity of the cardiac action and a feeling of faintness and dyspnea upon exertion. She had never been strong. She had had measles, chickenpox, pertussis and pneumonia in childhood. During her twelfth year she had several attacks of fainting and was unable to attend school. During the last two years she has had fainting spells which were responsible for several falls, in one of which her left arm was broken. Three times within two years she has attempted to take training for the nursing profession, only to be sent home after a few weeks, because of her health. From the last hospital training school which she attended, she was

discharged with a diagnosis of mitral disease. She has consulted many physicians. Several specimens of sputum have been examined without the discovery of tubercle bacilli. Once a diagnosis of pulmonary tuberculosis was made roentgenologically. Epilepsy has been diagnosed. Tonsillectomy has been done. Strychnine has been taken over long periods of time; under this therapy she became sick and restless.

The patient was a thin sickly young woman with moderate cyanosis of the lips. There was no evidence of disease of the lungs. The left border of the heart was 7½ cm. to the left of the midsternal line; the right 1½ cm. to the right. A systolic murmur was heard over the precordium, most distinctly at the base and over the left side of the back to the inside of the scapula and below it. Except that the lower pole of the right kidney was palpable the abdomen was negative. Normal reflexes were present and pathological reflexes were not elicited. The cardiac rhythm was regular, the rate 112 (after entering the hospital the rate varied between 90 and 100), the blood pressure was 130/90. The blood count was essentially normal. The urine was negative. The basal metabolic rate was — 4.6 per cent. The electrocardiogram showed normal mechanism with a diphasic T in Lead *2*, a negative T in Lead *3*, slurring near the apex of the R-spike in Lead *2* and deep splitting of R in Lead *3*. Roentgenological examination of the chest showed a heart of normal size slightly displaced to the left; the right border showed indistinctly, which was attributed by the roentgenologist to pleuro-

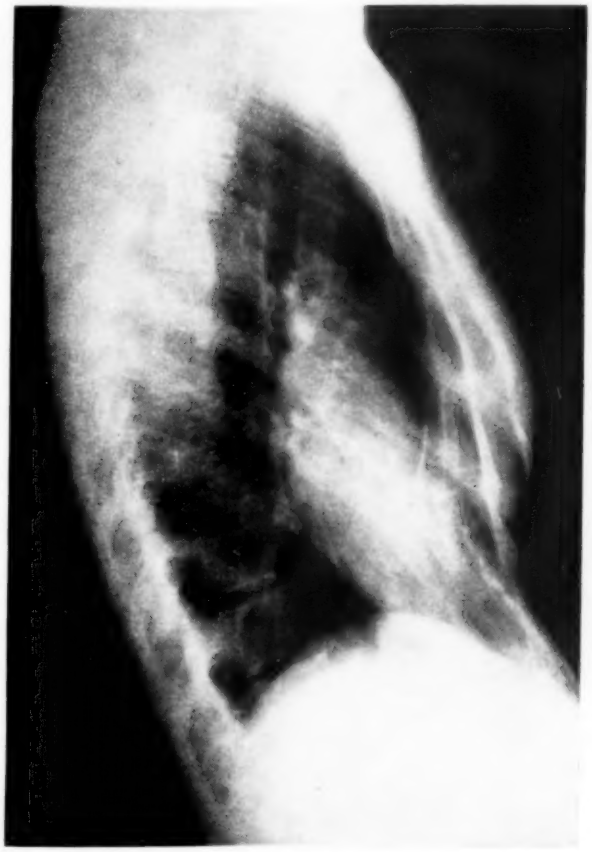

FIG. 1. Lateral roentgenogram of the chest of the first patient, who was operated upon.

pericardial adhesions, although fluoroscopically free movement of the heart was demonstrated. The lateral plate showed marked depression of the sternum. The distance from the eleventh dorsal spine to the point of maximum depression of the Trichterbrust measured 13 cm.

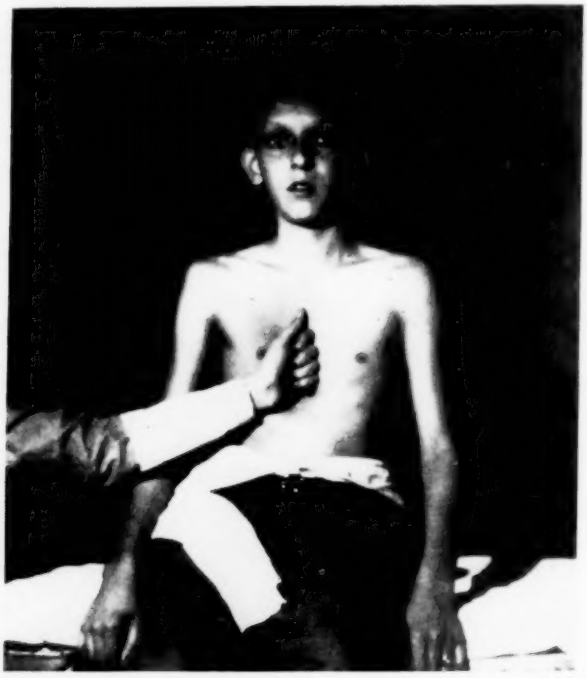

FIG. 2. Photograph of the second patient.

After ten days of observation this patient was operated upon by Dr. Jerome Head. "On the left side the 3rd, 4th, 5th, 6th and 7th costal cartilages were removed and on the right side the 4th, 5th, 6th and 7th. The lower one-half of the sternum together with the xiphoid was resected. The pectoral muscles were drawn together in the midline over the upper half of the defect. The fascia and subcutaneous tissues were closed similarly over the lower part of the defect. At the beginning of the operation the pulse rate was 100; coincident with the removal of the cartilages on the left the pulse dropped to 80 ... When a finger was inserted beneath the sternum the heart pressed tightly against it from behind, especially at the lower end and behind the xyphoid." Following the operation the cardiac rate fell to 70 to 80 and remained so for a day, then slowly went up over two or three days to 120 and receded within a few days to 80 to 90.

Four weeks after her discharge the patient reported that she had lost her cardiac consciousness and was walking a mile or more daily. After another three months continued improvement was reported. At this time the murmur noted prior to operation was confined to a small area about the second and third interspaces to the left of the sternum. Nine months after the operation she was seen again. At this time she was not doing so well. The original cardiac symptoms were not present but the patient was nervous and had lost some weight, (following the operation she had gained). An unhappy domestic situation was probably responsible for the nervous symptoms then present.

The *second* case was that of a boy of 1

years, who was referred to us from the Children's Memorial Hospital, where he had been under treatment for hemorrhage from a duodenal ulcer. The patient when first seen was cyanotic and moderately short of breath. He weighed 78½ pounds. The temperature was 97.8; pulse, 84; respirations, 20. The blood count was normal. The distance from the second thoracic vertebra to the sternum was 10 cm.; the anteroposterior diameter at the point of deepest depression was 8 cm. The width of the depression was 11 cm.; the depth, 4 cm.; and the vertical diameter, 14 cm. The apex was in the fifth interspace, 10½ cm. to the left of the midsternal line; the apex rate was 84; the blood pressure, 104/82. The X-ray plate showed displacement of the heart to the left and a widening of the transverse diameter. Three months after the first examination the cyanosis was rather less marked, the dyspnea definitely less. Operation has been discussed with the father but not urged; we are not yet sure enough of our ground to urge surgical interference without such symptoms as may be regarded as making an operation mandatory if the patient is to live without actual distress.

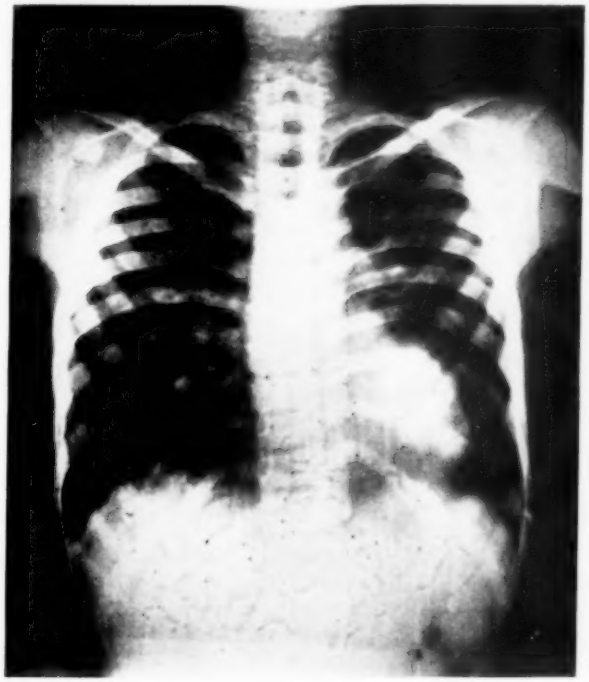

FIG. 3. Antero-posterior roentgenogram of the chest of the second patient.

SUMMARY

1. Trichterbrust is the term applied to a characteristic deformity of the sternum, with depression thereof, resulting in pressure upon the heart, usually with displacement. Definite cardiac symptoms are not the rule in these cases, but such do occur. Dyspnea and palpitation are the most common symptoms.

2. Operative procedures have been reported, especially in recent years, with good results. Another case is here reported in which operation was followed by prompt amelioration of

the symptoms. A smooth post-operative course, such as this patient presented, is not always to be expected. Since the operation reported, Dr. Head has operated upon another patient, not mine to report, who died within forty-eight hours following the operation.

3. In anticipation of operation, care should be taken to differentiate the cardiac effects of the deformity from the cardiac symptoms of the habitus asthenicus. Only in case the symptoms may reasonably be attributed to the former is surgical treatment justifiable.

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An Unusual Speech Disorder following Encephalitis Lethargica: Its Interpretation and Therapeutic Management

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IN reviewing the various sequelae of encephalitis lethargica reported by observers one is surprised at the multiplicity of phenomena in the different spheres of human organization. The sensory system in general, the special sensorium, the motor-system at its various levels, the vegetative sphere, the sympathetic nervous system, finally the psychic functions in general, including the affective status, may all isolatedly or conjointly become involved. Data are continuously accumulating. Many varieties of tic-like movements and analogous hyperkinetic manifestations have been observed and described. Some of them are relatively frequent, such as oculogyric crises; other manifestations are more or less rare, such as speech disturbances. Since 1922 there have appeared occasionally in the literature cases in which the tongue would be involved, namely propulsion followed by retreat, frequently or continuously repeated.[1] Smacking of the lips or continuously moistening the lips,[2] contraction of the muscles of the tongue between the teeth,[3] and vibratory or myoclonic contractions of the tongue have also been reported. In W. Sterling's case,[4] there was a linguo-salivary symptom: perpetually vibrating tremor alternating at times with paroxysmal trepidation of the myoclonic type so violent that saliva would run out of the mouth. The manifestations presented by the two patients described below are exceptional, and perhaps have not been observed before. They concern the buccal cavity, lips, chin, and especially the tongue which renders the speech unusual. This condition presents an additional postencephalitic phenomenon among the large number already observed. The cases here described are excellent examples for a somewhat different interpretation of affective manifestations in a condition which, generally speaking, has an organic basis, with the result of favorable therapeutic management.

Read, and patients exhibited, at the January meeting of the Philadelphia Neurological Society, 1932.

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Case Reports

Case I. S. S., female, age 17. Four years ago, following a slight febrile condition, she began to observe a mild impediment of speech. This condition progressed and became more and more pronounced for a time, but for the last two years the condition has been stationary.

Her present condition is as follows: In

speaking her tongue has a tendency to protrude between the teeth. In the beginning of her speech, the tongue rolls, curls, and places itself mostly on the right side. The muscles near the angles of the mouth and those of the chin contract more than the other muscles of the cheeks so that two deep furrows appear on both sides of her mouth. It seems that all the other muscles of her face remain immobile while the lip muscles function. This is observed in the beginning of her attempts to speak. The speech itself becomes indistinct; the tongue is always in the way. It may give the impression of stammering, but it is not. There is no evidence of aphasia, or paraphasia, of anarthria or dysarthria.

There is also noticeable, while speaking, a peculiar state of the lower jaw, namely a tendency to droop so that she frequently puts her hand under her chin to hold it up. While there is no paralysis of the tongue, as it can move in all directions, nevertheless the food remains in the mouth a long while and at times there is some difficulty in swallowing. The patient also complains of pronounced salivation. Examination of the buccal cavity fails to reveal any motor or sensory involvement of the muscles of palate and pharynx.

About six months ago the patient says she began to observe a gradually oncoming weakness of the right upper extremity. Examination reveals a certain amount of weakness of every segment of that limb and a fine tremor of the hand. She claims to have difficulty in threading a needle or doing other fine work.

Further examination shows increased kneejerks but no other pathological reflex. In respect to serology, blood, eyes, sphincters, and sensations there are no abnormalities.

Case II. J. B., female, age 19, had five years ago an attack of a depressive psychosis, from which she made a complete recovery. Two years ago, following a slight febrile state, she developed a speech disorder from which she is suffering now. One year later she developed a tic of the palpebrae.

The onset, mode of development, progressive course and the present state of the speech difficulty, are all identical with those of the first case; except that they are more pronounced. The position of the tongue, the condition of the muscles of the angle of the mouth and of those of the chin are also the same as in the first case. In addition to this, the patient also complains of food and liquids running out of her mouth during mastication.

It is interesting to note that this patient like the first one also presents a weakness of the right upper extremity in every segment of it. Her grip of the right hand is 50 and in the left 60 on the dynamometer, although like the first patient she is right handed. A detailed examination shows that in every other respect this patient is normal somatically.

If the two cases are postencephalitic it is to be presumed that the speech disorder like all the other sequelae reported in the literature is due to a lesion in the striatum with the usual structural damage. A question arises as to the possibility or impossibility of explaining the distorted speech on this purely organic basis. It is indeed difficult to admit that a direct injury to the striate body would be the sole cause of so many somatic, vegetative, and psychical manifestations as constitute the various groups of postencephalitic manifestations. A close examination of the mode of speaking of these patients leads to the conception of a purposeful pattern which originated four and two years ago respectively and remained as such up to the present. Both patients had difficulties of an affective character at the onset of the disorder and as an outlet from the states of anxiety in which they found themselves they developed a substitution or a compensation phenomenon in the form of a compulsion neurosis.

Discussion

An analysis of the identical peculiarity of speech in both patients does not permit one to classify it as a manifestation of aphasia or paraphasia, anarthria or dysarthria. The typical symptoms of the latter are not existing. Besides, the mode of onset, the lack of an acute insult to the parts of the central pathways of speech, the absence of phenomena which usually accompany organic speech disorders,—all these data are absent in the histories of our patients. A close examination of all the peripheral elements which enter into the formation of syllables and words in speech shows that the disorder lies in the improper and abnormal use of the many small muscles which are at work in the enunciation of words. The irregular display of the muscles of the tongue, lips, of the angles of the mouth, and of the chin described above, are sufficiently striking to exclude the possibility of organic dysarthria or aphasia.

Hypertonia or dystonia and hyperkinesia are very frequently met with in encephalitis lethargica and are quite characteristic of postencephalitic parkinsonism; these muscular phenomena may be generalized or limited to circumscribed areas. In our cases there was a history strongly suggestive of a brief attack of encephalitis and as a sequela there remains an irregular muscular function confined to the peripheral agencies used in the formation of letters, syllables, and words.

When an attempt is made to find an explanation of this speech disorder, one naturally turns first of all to the pathological substratum commonly found in the parkinsonian syndrome. Although lesions have been found at many levels of the brain, cerebellum, medulla and even spinal cord, nevertheless the striatal region occupies the center of attention. In fact almost all the varieties of postencephalitic phenomena have been explained on the basis of damage to the striatum. If motor or sensory disorders, hypertonic or dyskinetic disturbances may be due to an interruption in the structural connection of the striatum with various important segments of the central nervous system, thus explaining directly the anatomophysiological morbid manifestations, it leaves us in total ignorance with regard to the complex psychical phenomena which are so frequently observed in postencephalitic states. Alterations of character, disposition, behavior, radical changes in the affective state have been so frequently recorded! Are we in a position to speak of the striatum as a center for affective-psychic functions? Even if we could indulge in such a speculation, would this cover the ground? Could it explain why the postencephalitic individual blinks his eyes, and turns his eyes only in a certain definite direction in cases of oculogyric crises? Can it explain why in our two patients the speech is particularly disturbed when they meet strangers or when they are called upon to answer questions or when they have to participate in games, plays, etc.? The second patient relates that the speech disorder developed first, blinking of the eyes followed when the former began to improve. Presently both phenomena appear simultaneously; one reinforces the other when the patient attempts voluntarily to improve one of them. To content oneself with the

statement that the striatal system alone is the causal factor in all the varieties of affective or psychical abnormalities following an attack of encephalitis, would not be scientific.

In our two cases the speech disturbance and in one of them also the association of the eye blinking with the speech are closely connected with certain affective situations in the past as well as in the present.

Patient S. S. was obliged to leave the regular school unfinished to prepare herself for a salaried job in order to help out her relatives. She was in a state of great anxiety about the uncertainty of her heroic efforts. She deprived herself of necessities in order to accomplish her purpose. She is still working in this direction. In the midst of such an anxiety state and evidently because of it, she developed a tendency to walk, act and talk rapidly. She would become irritated, would make extreme efforts to refrain from giving sharp answers, from insulting the people who helped her financially during her preparation period. In addition to this there is another anxiety element in the life of this patient. Because of her home situation she is unable to participate in the pleasures of life: she is obliged to deny herself attending parties, dances, excursions to which she has been frequently invited. When occasionally she visits her friends and finds herself in a crowd she is seized with fear of not being able to keep up with the rest. Her speech becomes then particularly indistinct.

In patient, J. B., there is also a history of a state of anxiety but of a different origin. About the time of her brief attack of encephalitis, she led a life of extreme comfort, without even being forced to apply herself in acquiring knowledge. At the early age of 15 she received considerable attention on the part of her friends. One of her boy friends became unusually friendly and began to court her. She showed great fondness for him. At the time of her encephalitis her parents forbade him to call. The boy never returned. Having found out the cause of his abrupt abandonment of her, she had a number of violent altercations with her father. She became depressed, isolated herself, and could not sleep. In order to help her out the parents gradually induced her former friends to resume their friendship and to show her the same attention as before her illness. She then noticed a gradually oncoming difficulty of speech. At first it would occur only in the presence of male friends but later also in the presence of females. When therapeutic attempts were made to improve her speech, the blinking of the eyes would appear. Gradually both conditions became fixed and presently both phenomena are simultaneous. She is greatly depressed, refuses to appear in public and the unintelligent comments of her parents on this disorder contribute to its deeper fixation.

We observe a state of anxiety in both patients. In the first case, the fear of being unable to accomplish what she set out to do, also the long isolation and the shut-in existence which made her exceedingly shy and fearful of not being able to entertain and converse with people who made friendly advances to her finally led to the development of a compulsion neurosis in the form of a distorted speech.

In the second patient, the sudden abandonment of a male friend rendered her much depressed. She remained in this state a long time, refused new associations and finally when an effort was made by the parents to correct the situation, the patient began to hesitate in addressing others and thus developed the compulsion neurosis in the form of a distorted speech and later on of blinking as if she felt embarrassed in the presence of people and could not look straight in their eyes.

Both phenomena, the distorted speech and the blinking movements, are of the same order; they are defence reactions against an unconscious command. It is therefore evident that the compulsive phenomenon in both cases is a purposeful pattern and it originated from sources of an affective nature. The serious subjective state of both patients is their great anxiety which stands out as a conspicuous exteriorization of their inner life in the form of psychomotor phenomena of a compulsive character. The purpose behind the tongue or eye movements is self-evident. The latter merely represent a physical maladaptation phenomenon or a compulsive behavior reaction in the lives of two organisms. To understand fully an organism in its activities it is absolutely necessary to view it not merely as a structure but also, and especially, to see its background at all levels of its adaptive ability. A functional purposive level will always be revealed. If such a conception of compulsive situations is admitted by the therapeutist, some favorable results may be expected from a judicial application of the principles discussed above. In the two cases described above the fact of an organic insult to the midbrain and particularly to the striatum could not be altogether denied. It was also evident that the exclusive acceptance of an organic structural substratum disarms one from any attempt to remedy the morbid situation. On the other hand, granting the existence of a pathological lesion, if an effort is made also to consider the inner life of these patients and what lies at the main nucleus of their anxiety state, thereby directing attention more to the positive side of the situation, therapeutic results may be expected. Such a procedure brought fruit in our two patients, when we succeeded in demonstrating to them the logical connection of their anxiety with the affective experiences in their life. Progressive improvement is noticeable in spite of the possible existence of an organic lesion.

SUMMARY

An unusual postencephalitic sequela is described as observed in two patients. Attention is called to the fact that in addition to an organic lesion ordinarily found in encephalitis there are other factors of a functional character which may elucidate the nature of the multiple postencephalitic disorders observed so frequently. An organic lesion *per se* will not explain its *modus operandi* in creating all these disorders, especially those of an affective character. Recognition of this principle is of high value in therapeutic endeavors. The two cases described present an excellent illustration of this contention. The occurrence of the speech disorder described adds another, though rare, phenomenon to the large number of postencephalitic sequelae already known.

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Introduction to Clinical Medicine

"HISTORY taking, one of the most important disciplines of medical training, should familiarize the student with the life history and distinctive features of the onset, symptoms, and course of at least the common diseases and those with which they are most likely to be confused. It is very important that this early period of preliminary clinical training should be under the direction and supervision of the older and experienced members of the faculty, in order to secure the most satisfactory results and to establish a sound basis for the subsequent work of the student. With an experience in history taking, physical examination, laboratory diagnosis, and the use of instruments of examination, the student should be prepared to begin the study of clinical medicine.

"Teachers of clinical medicine should make it clear to students that many of the special examinations made in teaching hospitals are to show the student how knowledge is acquired and to supply complete data on a given patient for the purposes of instruction, not as an illustration of the actual requirements of practice. The specialized examinations and instruments can only supplement, they cannot supplant or substitute for, the direct clinical study of patients. Probably the overemphasis on special examinations by recent graduates and the tendency for them to seek practice in a specialty is partly due to the wrong emphasis in their clinical teaching.

"Students should be made to realize from the beginning of their clinical studies that the diagnosis in a large majority of illnesses can be made on the basis of a searching history, a thorough physical examination, relatively simple laboratory determinations, and the thoughtful consideration of the problem presented. The needs of a majority of patients can be solved by well recognized, relatively simple clinical methods. Some patients present functional disturbances which require considerable patience, time, sympathy, and an insight into the factors responsible. Only a small proportion need the services of specialists for a diagnosis. The physician and the student should be aware, however, of the importance of these special examinations as supplementary aids to established methods of clinical study in certain instances. An important feature of practice is the discrimination and judgment the physician should use in the selection of the time and type of such supplementary aids."

(From the *Final Report of the Commission on Medical Education*, 1932; Willard C. Rappleye, A.M., M.D., F.A.C.P., Director of Study. Pages 197-198.)

Oral Administration of Metaphen in the Treatment of Gastric and Duodenal Ulcers

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THE opinion is at present generally held that many patients with ulcer belong to the spasmophilic-vasoneurotic type, and therefore antispasmodic drugs, such as atropine and belladonna, in conjunction with the Sippy diet, are used in the treatment of ulcers and nervous dyspepsia. However, it is the opinion of the author (and also that of many other neurologists) that more attention must be paid to direct treatment of the stomach and the intestines, and that one should not rely exclusively on the above and on general methods of psychotherapy and physiotherapy, as, for instance, drug sedatives and stimulants. In the direct treatment of ulcers, the drugs commonly used are: sodium bicarbonate in large quantities, chalk of magnesia, bismuth preparations and silver nitrate. Tincture of iodine in five drop doses in a wine glass of water has also been recommended.[1]

Early in 1928, the author began administering to psychoneurotic patients who present symptoms of chronic abdominal distress, 3 c.c. of the 1:500 solution of metaphen, with most gratifying results. In fact, the author feels that a more rapid cure of the psychoneurotic state has been thus obtained in almost every case, than he has been able to accomplish by any other method. His opinion is based entirely on personal experience, as no literature concerning the use of metaphen in the treatment of gastro-intestinal disturbances, is as yet available.

Metaphen, an organic mercurial, was elaborated by Dr. George W. Raiziss[2,3] after an extensive study of chemical compounds involving the nitro-benzene-mercury complex. Metaphen, which is 4-nitro-anhydro-hydroxy-mercury-ortho-cresol, possesses, according to Dr. Raiziss, greater germicidal properties than mercuric chloride and many other antiseptics, being especially destructive for stapylococci and other bacteria of the same group; its bactericidal effect on other microorganisms is also very high. This is especially true of spore-bearing bacilli, such as *bacillus subtilis* and anthrax.

Recently, Konrad E. Birkhaug[4] also studied the bactericidal and bacteriostatic properties of metaphen, which was found by him to possess unusual disinfecting and antiseptic powers far in excess of mercuric chloride and other commonly used antiseptics. When *staphylococcus aureus* was used as the test organism, metaphen had a phenol coefficient of 1,500. Metaphen

was 400 times more efficient than mercurochrome against *staphylococcus aureus* when dissolved in equal parts of human serum and broth. It inhibits the growth of *staphylococcus aureus* after 48 hours incubation in a dilution of 1:16,400,000 while mercuric chloride accomplishes the same in a dilution of 1:32,000. The action of most antiseptics is greatly diminished in the presence of proteins. Hirschfelder and Wright[5] made an excellent study of the colloid chemistry of antisepsis and chemotherapy, and the effect of certain antiseptics upon proteins. In this study, the authors state:

"Metaphen did not produce any noticeable changes in the ultramicroscopic appearance either of egg albumin or plasma, presumably because it has but little affinity for the plasma proteins."

The following table indicates that the toxicity of metaphen is comparatively low when given per os. The rabbit has tolerated from 15 to 30 c.c. of a 1:1,000 solution, so that the average maximum tolerated dose is about 24 c.c. per kilo of body weight.

The aqueous solution of metaphen, owing to its high bactericidal and bacteriostatic power and the fact that it does not precipitate proteins, has a wide range of application in many branches of medicine, surgery[6,7,8,9,10,11], obstetrics, dentistry[12,13], otolaryngology[14,15,16,17], ophthalmology, urology[18], and blood stream infections[19].

The author's experience of four years in the oral use of metaphen in gastro-intestinal cases, is summarized in the accompanying table, which gives an analysis of 82 cases taken from his records. These comprise 26 examples of gastric, and 56 of duodenal ulcers. Twenty-seven of these have had thorough x-ray studies; many have had test meal and microscopic study of gastric contents to confirm diagnosis.

The table lists each case by initials, giving age, sex, diagnosis, dosage, and comments regarding x-rays, laboratory tests, diets, and the length of time during which gastro-intestinal symptoms were observed, and present condition, January, 1932.

ORAL ADMINISTRATION OF METAPHEN SOLUTION 1:1,000 TO RABBITS

DATE	DOSE PER KILO OF BODY WEIGHT	TOTAL AMOUNT GIVEN**	RESULTS OBTAINED
3-5-24	20 c.c.*	65.6 c.c.	Survived
6-9-25	40 c.c.	98.8 c.c.	Survived
5-24-26	40 c.c.	112 c.c.	Died on 7th day
6-12-26	30 c.c.	66.6 c.c.	Survived
1-30-29	20 c.c.	37 c.c.	Survived
10-1-29	15 c.c.	37 c.c.	Survived
10-1-29	20 c.c.	49 c.c.	Survived
10-14-29	25 c.c.	66 c.c.	Survived
10-14-29	30 c.c.	69.9 c.c.	Survived
2-24-30	25 c.c.	78 c.c.	Survived

*1 c.c. of 1:1,000 solution is equal to 1 mgm. of metaphen.
**Figures in this column indicate amount actually given according to weight of animal, and only one dose was given.

The percentage of complete recoveries suggests a possible specific cure for peptic and duodenal ulcers. This will be proved by more extensive studies as other physicians report their observations.

EIGHTY-TWO PATIENTS TREATED WITH METAPHEN

NO.	NAME	AGE	SEX	DIAGNOSIS	CLINICAL COMMENT	DAILY DOSE OF METAPHEN 1:500	RELIEF NO. OF DAYS	DISCHARGED
1.	B.A.B.	44	M	Duodenal ulcer	Intermittent attacks for 20 years	3 c.c. 2 hr. p.c.	24	R*
2.	F.G.R.	40	M	Duodenal ulcer	X-rays: 4/23/26, shallow duodenal ulcer; 7/19/26, sub-total gastrectomy; 3/5/27, 2 ulcers on duodenal cap	3 c.c. 2 hr. p.c.	3	R
3.	H.R.	47	M	Duodenal ulcer	Suffering since Spanish-American War	3 c.c. 1 hr. a.c. and bedtime	5	R
4.	S.F.M.	62	M	Duodenal ulcer	X-rays: 3/22/28, very large excavating ulcer in cap	3 c.c. 2 hr. p.c.	3	R
5.	C.H.M.	40	F	Gastric ulcer	X-rays: 1928, ulcer lesser curvature of stomach	3 c.c. ½ hr. a.c.	3	R
6.	W.H.D.	60	M	Gastric ulcer	Blood pressure 214/120. Ulcer many years	3 c.c. 1 hr. a.c.	3	R
7.	W.S.	43	M	Gastric ulcer	Test meal showed gastric ulcer	3 c.c. 1 hr. a.c.	7	R
8.	R.S.	27	M	Duodenal ulcer	Ulcer several months	3 c.c. 1 hr. a.c.	3	R
9.	V.T.	31	F	Duodenal ulcer	X-rays positive	1.3 c.c. 2 hr. p.c. and bedtime	3	R
10.	B.C.	39	F	Duodenal ulcer	Typical symptoms. Exam. positive	3 c.c. 2 hr. p.c.	3	R
11.	W.S.H.	55	M	Gastric ulcer	X-rays: ulcer lesser curvature, size of a quarter. Test meal: R.B.C.S.	3 c.c. ½ hr. p.c. and bedtime	3	R
12.	W.C.	56	F	Gastric ulcer	X-rays, 1928: ulcer lesser curvature	3 c.c. p.c. and bedtime	3	R
13.	J.V.B.	52	M	Gastric ulcer	Many years typical symptoms	3 c.c. p.c. and bedtime	2	R
14.	W.W.S.	65	M	Duodenal ulcer	Definite symptoms and signs	3 c.c. 2 hr. p.c.	4	T*

*R=Recovered.
*T=Temporary.

NO.	NAME	AGE	SEX	DIAGNOSIS	CLINICAL COMMENT	DAILY DOSE OF METAPHEN 1:500	RELIEF NO. OF DAYS	DISCHARGED
15.	C.N.W.	50	F	Gastric ulcer	History of infection of foot	3 c.c. p.c.	50	R
16.	W.H.C.	51	F	Duodenal ulcer	Typical symptoms. Marked secondary anemia	4 c.c. 2 hr. p.c.	7	R
17.	F.F.	61	F	Duodenal ulcer	Intermittent positive signs for many years	4 c.c. 2 hr. p.c.	3	R
18.	W.H.C.	51	M	Duodenal ulcer	X-rays negative. All symptoms positive	4 c.c. 2 hr. p.c.	13	R
19.	P.D.VN.	43	M	Duodenal ulcer	Definite symptomatic diagnosis	4 c.c. 2 hr. p.c.	20	R
20.	W.E.T.	24	F	Gastric ulcer	X-rays. Symptoms not relieved by Sippy diet	4 c.c. ½hr. a.c.	7	R
21.	E.M.	32	M	Gastric ulcer	X-rays positive	4 c.c. t.i.d. p.c.	3	R
22.	J.H.C.	45	M	Gastric ulcer	X-rays positive. Sippy diet over long period of no avail	4 c.c. t.i.d. p.c.	3	R
23.	R.W.A.	45	F	Duodenal ulcer	Frequent vomiting several hours after each meal. Symptoms positive	2 c.c. t.i.d. p.c.	5	R
24.	M.B.M.	36	M	Gastric ulcer	Ulcer since World War	4 c.c. t.i.d. p.c.	3	R
25.	R.F.F.	57	F	Duodenal ulcer	X-ray positive, 1928	4 c.c. 2 hr. p.c.	7	R
26.	D.H.	19	F	Duodenal ulcer	X-rays positive	3 c.c. 2 hr. p.c.	14	R
27.	P.E.A.	39	M	Duodenal ulcer	X-rays positive, 7/19/29, negative, July, 1930	4 c.c. 2 hr. p.c.	3	R
28.	E.B.W.	53	M	Duodenal ulcer	X-rays positive, 1928; negative, 1931.	4 c.c. 2 hr. p.c.	3	R
29.	A.S.	25	F	Gastric ulcer	Test meal positive	4 c.c. with meals	3	R
30.	R.W.	33	M	Duodenal ulcer	X-rays, 4/15/22, positive. Vomiting 2 hrs. after meals	2 c.c. 2 hr. p.c. and bedtime	3	R
31.	J.P.	37	M	Duodenal ulcer	X-rays positive. Vomiting everything, even water	4 c.c. on rising 2 hr. p.c.	4	R
32.	F.F.	57	M	Duodenal ulcer	Years of distress three hours after eating	4 c.c. 2 hr. p.c.	3	R

NO.	NAME	AGE	SEX	DIAGNOSIS	CLINICAL COMMENT	DAILY DOSE OF METAPHEN 1:500	RELIEF NO. OF DAYS	DISCHARGED
33.	G.Z.	41	F	Duodenal ulcer	1½ years. Pain three hours after eating	4 c.c. 2 hr. p.c.	1	R
34.	R.E.VB.	24	M	Duodenal ulcer	Ulcer for 8 months. Loss of weight	4 c.c. 2 hr. p.c.	2	R
35.	J.A.	34	M	Gastric ulcer	X-rays negative excepting for spastic colitis. Constant nausea and pain immediately after meals	4 c.c. p.c. and bedtime	3	R
36.	E.L.D.	62	F	Duodenal ulcer	X-rays: cholecystitis and chronic colitis, 1924	4 c.c. 2 hr. p.c.	3	R
37.	M.H.	59	F	Gastric ulcer	X-rays positive. Lesser curvature. Sippy diet three weeks	4 c.c. 2 hr. p.c.	4	R
38.	E.C.	45	M	Gastric ulcer	Gastrectomy years ago. X-rays, 1929: large ulcer greater curvature of stomach. X-rays, 1931, negative	4 c.c.	3	R
39.	B.W.	34	F	Gastric ulcer	Vomiting immediately after meals for hours	1 c.c. 2 hr. p.c.	3	R
40.	C.H.	39	M	Duodenal ulcer	10 years typical symptoms	4 c.c. 1 hr. p.c.	6	R
41.	J.J.	32	F	Duodenal ulcer	Typical symptoms	1 c.c. 1 hr. a.c.	2	R
42.	B.J.G.	32	F	Gastric ulcer	Operated soon for a gangrenous appendix. Ulcer cleared up	4 c.c. 2 hr. p.c.	None	U*
43.	J.A.V.	47	M	Duodenal ulcer	Distress 3 or 4 hours for years	4 c.c. 2 hr. p.c.	3	R
44.	J.H.	20	M	Duodenal ulcer	Pain after each meal	4 c.c. 2 hr. a.c.	7	R
45.	J.H.T.	73	M	Duodenal ulcer	Typical signs for many years	4 c.c. 2 hr. p.c.	3	R
46.	A.C.	44	F	Gastric ulcer	Typical symptoms with vomiting	2 c.c. 1 hr. p.c.	5	R
47.	A.M.S.	89	F	Duodenal ulcer	Typical symptoms 2 years with great loss of weight	1 c.c. 2 hr. p.c.	3	R
48.	M.O.J.	43	M	Gastric ulcer	Typical signs with loss of weight 3 years	4 c.c. 1 hr. a.c.	3	R

*U=Unimproved.

NO.	NAME	AGE	SEX	DIAGNOSIS	CLINICAL COMMENT	DAILY DOSE OF METAPHEN 1:500	RELIEF NO. OF DAYS	DISCHARGED
49.	C.H.	37	M	Duodenal ulcer	Typical signs	4 c.c. 1 hr. p.c.	3	R
50.	F.M.	58	M	Gastric ulcer	Typical signs with great loss of weight	4 c.c.	3	R
51.	L.B.	45	M	Gastric ulcer	4 years pain and pressure after meals	2 c.c. 15 min. a.c.	3	R
52.	L.C.	41	M	Gastric ulcer	2 years typical symptoms	4 c.c. ½ hr. a.c.	3	R
53.	M.G.B.	36	F	Gastric ulcer	X-rays positive	4 c.c. 2 hr. p.c.	9	R
54.	M.B.	51	F	Gastric ulcer	X-rays positive, 1928. Test meal positive. Vomited about 1 oz. of blood after meals	4 c.c. 15 min. a.c.	3	R
55.	H.L.C.	38	F	Duodenal ulcer	X-rays positive. 1 year with great loss of weight	2 c.c. 2 hr. p.c.	2	R
56.	E.C.S.	51	F	Duodenal ulcer	Positive signs for many years	4 c.c. 1 hr. a.c.	3	R
57.	J.A.S.	51	M	Duodenal ulcer	7 years immediate relief	1 c.c. 2 hr. p.c.	42	R
58.	L.S.VZ.	45	F	Duodenal ulcer	Several abdominal operations without relief	2 c.c. 1 hr. a.c.	3	R
59.	J.S.	42	M	Duodenal ulcer	Typical symptoms for 3 years with great loss of weight	4 c.c. 2 hr. p.c. and bedtime	3	R
60.	A.R.	67	F	Duodenal ulcer	Positive signs since 1922	2 c.c. 2 hr. p.c.	10	R
61.	S.C.	72	F	Duodenal ulcer	Living on modified Sippy diet for many years	2 c.c. 2 hr. p.c.	3	R
62.	J.F.J.	25	M	Duodenal ulcer	Typical symptoms for 2 years	4 c.c. 2 hr. p.c.	3	R
63.	W.T.	24	M	Duodenal ulcer	Typical symptoms	4 c.c. 2 hr. p.c.	3	R
64.	J.A.S.	48	F	Duodenal ulcer	On modified Sippy diet for 6 months	2 c.c. 2 hr. p.c. and bedtime	3	R
65.	F.M.	33	M	Duodenal ulcer	Typical symptoms	4 c.c. 2 hr. and bedtime	3	R
66.	R.H.C.	76	F	Gastric ulcer	Diarrhea caused by each meal	4 c.c. 15 min. a.c. and bedtime	5	R

NO.	NAME	AGE	SEX	DIAGNOSIS	CLINICAL COMMENT	DAILY DOSE OF METAPHEN 1:500	RELIEF NO. OF DAYS	DISCHARGED
67.	D.H.F.	45	F	Duodenal ulcer	Distress 4 hours after eating	4 c.c. 2 hr. p.c.	3	R
68.	S.R.	61	M	Duodenal ulcer	Coal tar stools since 1900	4 c.c. 2 hr. p.c.	5	R
69.	W.H.T.	50	M	Duodenal ulcer	Typical distress	4 c.c. 1 hr. p.c. and bedtime	3	R
70.	J.S.	36	M	Duodenal ulcer	Typical symptoms	4 c.c. 2 hr. p.c.	1	R
71.	K.P.	61	F	Duodenal ulcer	X-ray positive	2 c.c. 2 hr. p.c.	3	R
72.	E.S.	40	F	Gastric ulcer	Has had 4 major abdominal operations with no relief	4 c.c. 2 hr. p.c. and bedtime	1	R
73.	F.P.K.	42	M	Duodenal ulcer	Pain 4 hrs. after eating for years	4 c.c. 2 hr. p.c. and bedtime	1	R
74.	R.S.C.	44	M	Duodenal ulcer	Typical pains 1 year	4 c.c. 2 hr. p.c. and bedtime	3	R
75.	C.H.C.	55	M	Duodenal ulcer	Pain 4 hr. p.c. and 2 A.M.	4 c.c. a.c. and bedtime	3	R
76.	A.L.M.	72	M	Duodenal ulcer	Pain 3 or 4 hr. p.c. and 1 A.M.	4 c.c. 2 hr. p.c.	1	R
77.	G.B.	73	F	Duodenal ulcer	X-rays show 2 ulcers in bulb	4 c.c. 2 hr. p.c.	1	R
78.	J.D.	48	M	Duodenal ulcer	Chronic alcoholic	4 c.c. 2 hr. p.c.	1	R
79.	S. VanB.	44	M	Duodenal ulcer	I year pain 3 or 4 hr. p.c.	4 c.c. 2 hr. p.c.	3	R
80.	E.C.B.	61	M	Duodenal ulcer	X-rays positive, also spastic colitis	2 c.c. 2 hr. p.c.	3	I*
81.	H.B.	35	F	Duodenal ulcer	X-rays positive. Vomits even water	4 c.c. 2 hr. p.c.	1	R
82.	I.S.	51	M	Duodenal ulcer	Pain 2 to 4 hr. p.c.	4 c.c. 2 hr. p.c.	1	R

*I=Improved.

In searching for the fate of the metaphen taken orally, the laboratory has found large traces of mercury in the stool, but none whatsoever in the urine or blood.

Toxicity of any type has in no case been demonstrated, and the author has had many patients who have continued metaphen at the dosage of 16 c.c. daily for months without reporting to him—patients who felt so well that they were afraid to discontinue treatment for fear of recurrence of gastro-intestinal disorders.

In 1929, the author increased the dose to 4 c.c. three times a day, and since then no further increase has been necessary to obtain relief from either pain, pressure or other distress in the abdomen due to gastric ulcer, duodenal ulcer, chronic ulcerative colitis, or other types of colitis. About half of his patients have taken the prescribed dose of the 1:500 solution of metaphen diluted with equal parts of either glycerin or cinnamon water in half a glass of water directly before or after meals in cases of gastric ulcer, or one hour before or two hours after meals in cases of duodenal ulcer. In colitis, metaphen has been given directly after each meal and at bedtime in order that the drug might be carried throughout the intestines along with the food.

In practically all his cases, there has been relief from pain in three days' time on the average, regardless of the fact that most of the patients have suffered for years. Many have come to him with the diagnosis of nervous dyspepsia, vomiting everything taken by mouth, even water. The metaphen solution, however, was never vomited, and in one to three days the patients were able to eat large meals.

Usually when all pain or distress is relieved in the three day period, the author continues with three or four doses daily for one week, two doses daily the second week, one dose daily the third week, and then a dose every other day the fourth week, stopping the drug thereafter. It is interesting to note the large proportion of these cases, which have had no recurrence of their chronic gastro-intestinal symptoms since their treatment. Their nervous and mental symptoms have disappeared entirely and they have become readjusted to their environment.

X-rays taken before and after the oral administration of metaphen, have shown complete disappearance of the ulcers of the gastric and duodenal types. Chronic ulcerative colitis cases have become symptom-free in a very short time. Diarrheal stools, containing pus and blood, have ceased after the first day.

Most of these cases of ulcers had been on a strict Sippy diet or modified forms of it, and, in every case, the patients have been placed upon a varied diet; nevertheless, there has been no complaint or resulting pain or pressure.

It must be continually borne in mind that all of these cases involved psychoneurosis, either plainly hysterical in type, or they were suffering from anxiety or compulsion forms of neurosis. The psychoneurosis has apparently subsided as a result of the direct attack of metaphen upon the gastro-intestinal lesions.

A few of the more striking cases are now described:

Case Reports

Case No. I. Miss E. C., age 45, a clerk in a very responsible position. Chief complaint: distress in the entire abdomen.

Appetite poor. Bowels constipated. No sleep without sedatives. Suffering from a complete nervous breakdown since March, 1930, when her mother died suddenly in her arms. Came under the author's care after three months' treatment in a private clinic in a neurological institution. In 1905 both ovaries were operated upon for cysts. In 1914 she had four operations: the first was a gastro-enterostomy on account of gastric ulcers; the other three eventually resulted in a gastrectomy removing four-fifths of the stomach. At age 38 she experienced her menopause.

On July 7, 1930, a gastro-intestinal x-ray series showed another ulcer on the small remaining portion of the stomach. She was still suffering from psychoneurosis. She was given metaphen solution 1:500, 4 c.c. one hour before meals and at bedtime, diluted in an equal amount of glycerin. In three days the distress in the epigastrium had entirely disappeared, and in nine days she had gained seven pounds in weight.

X-rays of the stomach, April 6, 1931, showed no sign of peptic ulcer. She returned to work September 2, 1931, and has not lost any more time. She has never had any return of the epigastric pain. Her nervous condition has entirely disappeared.

Case No. II. E.B.W., male, age 53, occupation, proprietor of laundry. Chief complaint, distress in epigastrium two hours after each meal.

He was a case of profound psychoneurosis. On April 24, 1930, he was given 4 c.c. of the solution of metaphen, 1:500, with an equal amount of glycerin two hours after meals. In three days there was no more distress, and he felt like a new man. April 29, 1930, the dose of metaphen was reduced to 2 c.c. X-rays of his gastro-intestinal tract taken in 1928, in October, 1929, and March, 1930, all showed ulcer of the bulb of the duodenum. X-rays taken June 27, 1930, showed the ulcer greatly improved. The x-ray report dated June 27, 1930, was as follows:

"Duodenum: First portion is fairly large and at times filled completely, with a normal outline; at other times there was a tendency to trefoil deformity. Comparing these with previous radiographs made in March, this year, elsewhere, we find that the duodenal cap at this time fills decidedly better and that the deformity noted on the mesial aspect has practically entirely disappeared. The deformity noted in prepyloric ulcer is generally organic. The deformity noted in postpyloric or duodenal ulcer is generally due to spasm unless a niche or accessory pocket is found. We note that at the previous examination in March, the doctor reports that the duodenal cap was not unduly tender on pressure. At this time we do not find any marked tenderness, but there is definite tenderness noted over the duodenal cap that is not found elsewhere. However, we feel that so far as the deformity of the cap, which is the result of spasticity, is concerned there is definite improvement between March and the present time."

X-rays made in April, 1931, showed no lesion of the stomach or duodenum; and his psychoneurosis had been cured.

Case No. III. P.E.A., male, age 39, occupation, certified public accountant. Chief complaint, complete nervous breakdown. This patient has not worked for three years, and complains of distress two to four hours after each meal. X-rays, July 19, 1929, showed ulcer of the duodenal bulb. He was given 4 c.c. of metaphen solution, 1:500, with equal amounts of glycerin two hours after meals, and in three days the epigastric distress was entirely gone. He returned to work immediately and has continued to be employed without interruption to date. X-rays taken in July, 1930, showed no evidence of duodenal ulcer. His psychoneurosis disappeared with the cessation of epigastric distress.

Case No. IV. Mrs. W. C., age 56, occupation, advertising manager of a department store. Chief complaint, vomiting after meals and nine hemorrhages from the bowels shown by profuse coal tar stools since October, 1927. January 31, 1929, she was in a state of profound psychoneurosis. X-rays of the gastro-intestinal tract in March, 1928, dem-

onstrated an ulcer of the lesser curvature of the stomach. February 11, 1929, she began to take metaphen solution, 1:500, 3 c.c. in cinnamon water immediately after meals and at bedtime. In three days the gastric distress, vomiting, and symptoms of psychoneurosis disappeared. On March 11, 1929, she was able to stop metaphen and has had no need of any medication whatever to date.

Case No. V. W. S. H., male, age 55, occupation, sales manager, constantly travelling throughout the United States. Chief complaint, constant pain in epigastrium aggravated by food. This patient was profoundly neurasthenic, introspective and apprehensive. X-rays, December 18, 1928, demonstrated an ulcer the size of a twenty-five cent piece on the lesser curvature of the stomach. Gastric analysis showed red blood cells in all tests, normal otherwise. He was placed upon metaphen solution, 1:500, 3 c.c. in cinnamon water one-half hour after meals and at bedtime, and his report on the third day was that he was entirely relieved of distress after eating. His psychoneurosis has disappeared and he has never had any return of the gastric distress to date.

Case No. VI. S. F. M., male, age 62, occupation, retired. Chief complaint, vomiting attacks two hours after eating, loss of weight, and great nervousness. X-rays, March 22, 1928, showed a large penetrating ulcer in the duodenal bulb. He was given 3 c.c. of metaphen solution, 1:500, diluted in water two hours after meals, and his report on the third day was that he had not vomited since he began taking the metaphen. His nervousness was rapidly improving.

Frequent reports to date (October1, 1931) are of no recurrence of any signs of ulcer, and he has been absolutely well with no need of any medication whatsoever after the first month.

It now becomes of interest to consider the possible explanation of the beneficent action of metaphen, primarily a bactericidal agent, on gastro-intestinal ulcers. In this connection, it must be pointed out that recently the thesis has been sustained by several authors, that infection plays an important rôle in the evolution of many such ulcers. Extensive investigations in this direction have been carried out by Rosenow[20,21,22,23], who was able to demonstrate the presence of streptococci in several cases of duodenal and gastric ulcer. By injection of these organisms into dogs and rabbits he obtained ulcers resembling those in man in respect to location, gross microscopic appearance and in the tendency to become chronic, to perforate, and to cause severe and fatal hemorrhages. The same organism was isolated by him from ulcers in the hog, calf, cow, sheep and dog. These experiments were repeated by Celler and Thalhimer[24] who found that non-hemolytic streptococci are present in practically all gastric ulcers; these authors, however, do not regard this as proof that this organism is the factor which either initiates the ulceration or prevents healing; but the constant presence of streptococci in such lesions must have some significance which requires further elucidation.

A similar opinion is expressed by Duval and his co-workers[25,26], who ascribe to infection a secondary if not a primary rôle in the development of gastric ulcers. This view is supported by the following facts: While ulcers are usually regarded as evolving without fever, actually a subfebrile state or even an acute elevation of temperature will often appear during a gastric attack; the development of ulcers appears to be influenced by some epidemics and ulcers are frequently aggravated as a consequence of intercurrent infectious diseases. Hyper-

leucocytosis is often observed in patients afflicted with ulcer; thus, Girault[26] has found the number of leucocytes above normal in 23 out of 28 patients with ulcer confirmed by operation. Duval has found the intradermoreaction with streptococcus positive in 60 per cent of cases, while the number of leucocytes was above normal in 33 per cent of cases. Furthermore, inflammatory exacerbations in chronic ulcers, and the presence of bacteria in the wall of the ulcer, support Duval's thesis. Of interest is the fact that mortality following large excisions is less than that following small excisions. This apparently paradoxical fact seems to indicate the possibility that the small excision is within an infected zone.

Askanazy[27] has found the organism of thrush (*Oidium albicans*) in the tissues of operated gastric ulcers in 25 out of 30 cases. He has also succeeded in creating ulcers experimentally by the inoculation of animals with impaired mucous membrane of the stomach with this organism.

Smithies[28] in a study of the etiological factors associated with chronic gastric ulcer, has found that 137 out of 522 histologically proved ulcers, or 33.7 per cent, were associated with an infection.

It thus seems very probable that infection plays an important part in gastro-intestinal ulcer, and it is therefore not entirely irrational to expect that a strong bactericidal agent, which is at the same time non-injurious to the tissues in the solutions used should exercise a healing effect on ulcers. The patients' histories, here presented, show that such is the case.

Conclusions

1. Metaphen, in 1:500 solution, was given orally to patients with symptoms of chronic abdominal distress in the dose of 4 c.c. three times a day with very gratifying results.

2. The material presented includes an analysis of 82 cases, 26 of gastric and 56 of duodenal ulcers. Complete x-ray studies were made of 27 of these cases; diagnosis was also confirmed in many cases by test meal and microscopic study of gastric contents.

3. Relief from pain was obtained in practically all cases in an average of three days' time.

4. No toxic effects were ever observed.

5. Complete disappearance of gastric and duodenal ulcers consequent upon treatment with metaphen has been demonstrated by means of x-ray studies, made before and after treatment.

6. A possible explanation of the action of metaphen, primarily a bactericidal agent, may lie in the part played by infection in the evolution of ulcers of the type considered, as has been recently emphasized by several authors.

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The Rôle of the Bowel in Chronic Arthritis

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THE bowel is usually mentioned as a possible origin of the varied nerve, muscle, and joint syndromes characterizing chronic infectious or atrophic (American Committee for the Control of Rheumatism) arthritis. The colon has been taken to be a focus of infection, the source of bacterial toxins or the seat of autointoxication. Free action of the bowels has always been advocated in the treatment of arthritis. Numerous medicinal and mechanical measures have been elaborated to secure this. The adnexa of the bowel, the appendix and gall-bladder, have played prominent rôles as possible foci of infection. Fletcher and Graham[1] found the colon in chronic arthritis characteristically atonic.

The varied and varying flora of the bowel has been repeatedly studied in its relation to arthritis. Burbank,[2] Keating[3] and Crowe[4] have reported success in using vaccines of fecal organisms in the treatment of chronic arthritis.

Traut and Herrold[5] found streptococci much more commonly on the rectal mucosa of arthritic patients than in the rectums of controls. Since then the rectal flora of many more patients has been studied. The later results tally with those already reported. Streptococci, usually green, less commonly hemolytic, are found far more commonly in the rectums of arithritic patients than in normal controls and often are the predominatnig organisms in cultures made by our method. (Table I.) This method has been a great improvement over previous means of isolating bacteria not included in the bacterial population of normal individuals, the bacteria peculiar to the arthritic. The usual stool culture selects material from the bowel lumen or stool center, a medium unfavorable to the growth of a delicate streptococcus because of competitive bacteria, presence of bacteriostatic substances and lack of water.

Repeated cultures of the rectal wall have usually shown similar floras. To some extent the kinds of bacteria and their relative proportions have fluctuated with exacerbations and remissions of the patient's joint or gastrointestinal symptoms. Frequently I was able to confirm the opinion that with looser stools there was a higher percentage of streptococci. In some rectums staphylococci have been especially numerous. They are usually white staphylococci. Checks of our method have failed to demonstrate skin contaminations. As will be shown later many of these staphylococci are agglutinated strongly by serum from

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TABLE I
RECTAL BACTERIA IN ATROPHIC ARTHRITIS

NO. OF PT.	SEX	AGE	SEVERITY	STREPTOCOCCI	PER CENT OF STREPTOCOCCI	OTHER BACTERIA	GASTRO-INTESTINAL STATUS AND REMARKS
							Normal digestion
1	F	32	I	None	..	B. coli	Pulmonary tuberculosis
2	F	43	III	Green	5 to 90	B. coli Staph. albus	Alternating diarrhea and constipaton
3	M	33	I	"	60	B. coli	Constipation
4	F	27	I	"	20	B. coli	Spastic colitis
5	F	32	I	Hemolytic	15	B. coli	Spastic colitis
6	F	48	II	Green	5 to 30	B. coli	Fermentative colitis
7	F	48	I	"	5	B. coli	Irritable bowel
				Indifferent	5	Staph. albus 5%	Constipation
8	F	80	II	Green	10	B. coli	Cathartic colitis
9	F	44	I	"	20	B. coli	Constipation
10	F	46	I	"	10	B. coli	Constipation
11	M	35	I	"	10	B. coli	Constipation
12	F	46	I	"	10	B. coli	Constipation Irritable bowel
13	F	45	I	"	2	B. coli Staph. albus	Rheumatic purpura Ptosis
14	F	50	II	"	2 to 80	B. coli 10%	Severe irritable bowel
15	F	58	III	Indifferent	10	B. coli	Fermentative colitis
16	F	47	II	Green	7	B. coli	Unknown Constipation
17	F	72	III	Hemolytic	3	B. coli	Ptosis
18	F	48	I	None	..	B. coli B. coli 40%	Irritable bowel
19	F	52	I	Green	50	B. coli hem. 10%	Irritable bowel
20	M	27	I	"	10	B. coli	Normal
21	F	25	I	"	2	B. coli	Normal
22	M	46	II	"	10	B. coli	Normal
23	F	47	I	Hemolytic	5	B. coli	Constipation Ptosis
24	F	56	I	Green	50	B. coli	Constipation
25	F	58	III	None	..	Staphy. 30%	Inactive case with anchyloses
26	F	55	II	Green	10	B. coli	Ptosis Constipation
27	F	54	II	"	2	B. coli	Irritable bowel Constipation
28	M	29	I	None	..	B. coli	Chronic prostatitis Strep. virid. obtained
29	F	68	II	Green	2	B. coli Staphy. 40%	Chronic cholecystitis Chronic appendicitis
					10	B. coli	Green streptococci found after one month.
30	F	42	I	Hemolytic		Staphy. 2%	Hemolytic absent
31	M	32	I	Green	50	B. coli	Irritable bowel
32	F	50	I	Hemolytic	30	B. coli	Constipation
33	M	45	III	None	..	Staphy. 30%	Constipation
34	F	34	II	Green	33	B. coli	Constipation. Postoperative hypothyroidism.
35	F	54	I	"	4	B. coli	Fermentative colitis
36	F	24	I	"	2	B. coli	Normal

NO. OF PT.	SEX	AGE	SEVERITY	STREPTOCOCCI	PER CENT OF STREPTOCOCCI	OTHER BACTERIA	GASTRO-INTESTINAL STATUS AND REMARKS
37	F	37	I	"	4	B. coli	Irritable bowel
38	F	50	II	"	40	B. coli	Irritable bowel Hyperthyroidism
39	F	68	III	None	..	B. coli	Irritable bowel Constipation
40	M	42	I	Green	10	B. coli	Ptosis
41	F	60	I	"	2	B. coli	Constipation Constipation
42	F	64	II	"	50	B. coli	Irritable bowel
43	F	22	IV	"	30	B. coli	Irritable bowel
44	F	34	II	"	5	B. coli	Irritable bowel
45	M	37	I	Indifferent	10	Staphy. 50%	Spastic colitis Atonic ptosed colon
46	F	25	II	Green	50	B. coli	Pulmonary tuberculosis Chronic prostatitis Green streptococci found
47	M	35	I	None	..	B. coli B. coli	Hypothyroidism
48	F	60	I	Green	30	Staph. albus 10%	Constipation Peptic ulcer
49	F	58	II	Hemolytic	2	B. coli	Irritable colon
50	F	45	II	Green	5	B. coli	Irritable bowel
51	M	43	I	Green	15	B. coli 85%	None
52	M	46	I	Indifferent	1	B. coli B. coli 15%	Mucous colitis Constipation
53	M	47	II	Hemolytic	80	Staph. albus 5%	
54	F	53	I	Green	80	B. coli	Constipation
55	F	47		"			
56	F	22	IV	"	2	B. coli	Constipation
57		47	I	"	50	B. coli	Normal
58	F	62	I	"	1	B. coli	Constipation
59	F	22	I	"	2	B. coli	Constipation
60	M	37	III	"	50	B. coli	Constipation

arthritic patients. Vaccines made from them have acted as powerful antigens aiding the patients in recovery. Crowe has also isolated his *"micrococcus deformans"*, a white staphylococcus, from the stool.

The percentage of streptococci in the rectum bore no relation to the severity of the disease. Neither was the type of streptococci related to the variety or severity of joint disease except in one instance. In one case of rheumatic fever indifferent streptococci were repeatedly isolated from the rectum. The rectum of a patient with rheumatic purpura yielded five per cent to ten per cent of green streptococci on two examinations. Streptococci were rarely found in the rectums of patients with osteo-arthritis.

Other workers, as well as I, have found the streptococci of the mouth and teeth very similar, if not indistinguishable from the streptococci of the bowel. It is presumable that pathogenic bacteria resident in the mouth or ingested in food passing the more or less efficient and variable barrier of the bactericidal stomach secretions should enter the bowel unscathed. The bowel stasis described as characteristic of the entire gastro-intestinal tract by

Fletcher and Pemberton, would favor their absorption or the absorption of their toxic products. Arnold[6] has found *B. prodigiosus* in the blood after feeding it to guinea pigs. The subsequent involvement of joint or other tissues is a direct consequence. Rede-will, Potter and Garrison[7] mention the migration of streptococci from the bowel to teeth and tonsils.

The remarkable frequency of gastro-intestinal symptoms and findings in patients with atrophic arthritis stimulated me to investigate the relation of the gastro-intestinal disorders to joint disease. Care was taken to separate such localized diseases as cholecystitis or appendicitis. In most of the patients, abdominal symptoms were those commonly ascribed to irritable bowel, mucous or spastic colitis. Almost all had some intolerance to starch. Their digestive disturbances were much improved by reducing the gross starch of their diets. Fermentative colitis and its possible relation to Pemberton's disturbed carbohydrate utilization in these patients has recently been described by Monroe and Hall.[8] Under the fluoroscope the colons of most of these patients were dilated and atonic.

In my patients the gastro-intestinal complaints were so prominent as to demand dietary instruction as one of the very first measures in our broad attack upon the rheumatic disease. The relation between the gastro-intestinal dysfunction and the joint disease was obvious. Exacerbations of joint symptoms were coincident with relapses of the gastro-intestinal disease. The most common association was increase in the pain, stiffness and swelling of the affected joints together with increased abdominal pain, flatulence and loose stools. Constipation has been prominent in the complaints of most of my patients. Relief of constipation has always meant substitution of vegetables and fruits for foods of high carbohydrate and caloric value. Improvement has been much more marked by relieving constipation through dietary measures rather than by cathartics.

Seven of the sixty patients cultured showed no streptococci in the rectum. Nos. 28 and 47 had chronic prostatitis. Obvious foci had been removed from the other five patients previous to the rectal cultures. Patients 1, 18, 25, and 28 showed no streptococci on one culture. Patient 33 showed none on two examinations. Possibly further cultures in these cases would have shown streptococci. Patient 25 was a healed case in perfect health except for anchylosis of a hip and the vertebrae. Her active arthritis had terminated more than 15 years before.

The history of patient 13 is interesting. She first consulted me because of purpura. On this occasion no streptococci were obtained from the rectum. Thirteen months later she complained of stiffness of the neck associated with grating in the cervical vertebrae. These vertebrae were definitely tender. Coincidently streptococci were easily isolated from the rectum.

Hemolytic streptococci were first obtained from the rectum of Mrs. Br--. She was given five subcutaneous injections of a vaccine of those organisms. After 18 days no hemolyzing bacteria were detected. Coincidently her arthritis had disappeared.

The colon bacilli found have usually been of the non-hemolytic *communis*

type. In six instances hemolytic colon bacilli were isolated.

I have arbitrarily graded chronic arthritis into grades I to IV. Grade I comprises those with pain and little deformity or those with deformity of slight degree, not interfering with their occupation. Grade II includes those with more marked disability. Grade III embraces those with deformity in many joints but still allowing the patient to be about with much discomfort. Grade IV includes those completely disabled, the bedridden, and those able to be about only on crutches or in wheel chairs.

We have cultured the rectum in fifteen patients free from arthritis. Streptococci were found only in a patient with purpura of the rheumatic type, a syndrome allied to arthritis, and in two patients with chronic ulcerative colitis. Streicher and Kaplan[9] have called attention to the frequency of streptococci in the colons of patients with ulcerative colitis. Cultures were repeatedly made of the nonarthritic patients. Those without streptococci in the first examination did not have streptococci in subsequent examinations.

Relief of the arthritic symptoms and findings was usually coincident with a reduction of the number of streptococci in the rectum. In my opinion the improvement indicated a change in the "soil", a lessened susceptibility to its parasitic flora, as well as a reduction of invading pathogens.

Eighty-one per cent of my patients were women and of these seventy-one per cent were between 40 and 60 years of age.

In a few instances we encountered the difficulties in classification of chronic arthritis patients mentioned by Jordan and Boland.[10] Whether a patient had a recurrence of rheumatic fever or a flare-up of atrophic (rheumatoid) arthritis was occasionally difficult to ascertain.

The streptococci isolated were usually of the viridans type. They were usually in short chains. All retained the Gram stain. They were ovoid to round. Usually the individual bacteria were large. They frequently appeared in pairs, like an individual coccus or a diplococcus. Their broth cultures were diffusely clouded. Only rarely was it difficult to grow them in broth. Their colonies were originally all "smooth", with evenly round borders. Prolonged cultivation brought out dissociation. Colonies might not grow so distinctly green, approaching the indifferent or gamma group of Brown.

It is impossible to classify my strains of rectal origin according to the plan of Andrews and Horder[11]. According to them *streptococcus fecalis* ferments the same sugars as does *streptococcus salivarius;* namely, it ferments mannite but does not ferment raffinose or inulin. I have found no green streptococci in the bowel fulfilling these requirements. The green streptococci found fermenting mannite but not raffinose have also been resistant to bile and heat, placing them in the class of enterococci. The *enterococcus* and *streptococcus mitis* (Holman) predominate.

The green streptococci isolated from the bowel have usually been of low virulence for animals. One cubic centimeter of a 24-hour broth culture injected intraperitoneally does not kill

mice; and even in doses as large as 5 c.c., has failed to produce arthritis in rabbits. I discovered that arthritis could occasionally be produced by inoculating the streptococci into the colon. The same strains were without effect on intravenous injection.

Hemolytic streptococci were isolated from the rectums of four patients with atrophic arthritis. According to their fermentative ability they were *Streptococcus hemolyticus II* (Holman), *Streptococcus infrequens*, and *Streptococcus subacidus*. These streptococci have retained their extreme hemolyzing ability over one year of subculturing. Of any of these hemolytic strains, 0.5 c.c. of a broth culture is fatal to mice in 12 hours. The heart's blood of the dead mice was subcultured on blood agar plates. The washings of one of these plates proved fatal to rabbits in 5 to 14 days. Both purulent and non-purulent arthritis were manifested by these rabbits.

Some strains are conspicuously agglutinated by high dilutions of patient's blood. Extensive agglutination experiments suggest the inter-relationship of these various strains as well as their relation to the disease of their hosts. The isolated streptococci were usually agglutinated by their homologous sera. Certain strains were agglutinated by the sera of other patients in such high dilutions as to suggest an immunological relationship of the rectal streptococci found in arthritics.

Treatment

The serum of patients was routinely used in agglutination experiments against significant bacteria isolated from the rectum, from the interior and exterior of extracted teeth, from prostatic secretions or from the centers of excised tonsils. I included in these agglutinations long-studied strains agglutinated by the sera of other arthritics. I selected such as had proven effective antigens in the vaccine treatment of other patients as judged by the relief of the arthritic symptoms and the disappearance of the arthritic findings. The vaccines used were made of the organisms agglutinated by the patient's serum in high titer. For the most part these were streptococci of rectal origin.

Fifty-eight patients with chronic arthritis were observed sufficiently long to justify an appraisal of their treatment. These patients were followed for three years. Twenty-seven of these patients received no vaccine from me. Thirteen of these non-vaccine patients, or 48 per cent, recovered entirely or were greatly relieved. All of the patients, when first seen, are placed in the non-vaccine group. It is only after their failure to improve upon graded exercise, regulated rest, diet, massage and removal of foci, and after a careful bacteriological and immunological assay that they are subjected to vaccine treatment. Consequently the second group, the vaccine cases, really represent the more difficult patients, those remaining after non-specific measures have failed. Thirty-one patients were treated with vaccine. Twenty-one (68 per cent) of these were markedly improved or recovered. Four had almost no relief. One of these has osteo-arthritis. Osteo-arthritis is not recognized as an infection and is not accessible to treatment by bacterial antigens. Another was a

stenographer, badly crippled and terribly fatigued, managing to stay at work. She seemed "burned out", depleted of the elements necessary to recovery. She is now in remission, after cessation of vaccines, upon the institution of rest periods and the postural exercises of Goldthwaite and Osgood. A man, although badly crippled, sold goods from house to house. Like the stenographer, he was continually exhausted, unable to marshal sufficient energy or resistance to fight the disease. Four of the 31 vaccine patients made substantial improvements on subcutaneous administration of a suspension of the *Micrococcus deformans* of Crowe, and casein. Since the sera of these patients did not agglutinate the *Micrococcus deformans*, and no staphylococci were isolated from their foci of infection, improvement of these four patients must be credited to foreign protein.

A solution of casein was often combined with the streptococcus vaccine. Given alone it did not benefit any patient with arthritis. The combination was much more effective than either the streptococcus emulsion or the casein used in much larger amounts separately. Possibly the casein prepared the tissues, increasing their susceptibility to the bacterial antigen. As noted by Crowe the addition of a staphylococcus to the streptococcus vaccine enhanced its benefits. Crowe ascribes specificity to this staphylococcus effect. Again, a polyvalent vaccine of all the bacteria agglutinated by the patient's serum was successful where an autogenous vaccine failed.

Whether vaccine raises the resistance of the patient or desensitizes him to bacterial allergens, it has an important position in the treatment of chronic arthritis.

Summary

1. Rectal cultures in arthritic patients yielded streptococci more frequently and in larger numbers than did similar cultures in non-arthritics.

2. Streptococci isolated have for the most part belonged to the enterococcus group.

3. Agglutination by the serum of the host and cross-agglutination of other rectal strains are present.

4. Forty-eight per cent of a group of patients with chronic arthritis were markedly improved or recovered with the help of non-specific treatment.

5. Sixty-eight per cent of the patients treated with vaccines of the streptococci from rectal and other foci were markedly improved.

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Hygiene of the Soul by Maimonides
1135 to 1204 A.D.

"IT IS known to my lord, may God lengthen his days, that the emotions of the soul bring about great, general, obvious, definite changes in the body. One sees how a person of robust build, sonorous voice, and blooming complexion, when he suddenly receives news that troubles him exceedingly, at once his color becomes pale, his look softens, his posture stoops, his voice becomes weak, and if he should want with all his might to raise his voice, he is unable to do so, his strength weakens. He often trembles on account of weakness, his pulse beat becomes smaller, his eyes sink into their orbits. His eyelids become so heavy that they cannot move, the body surface becomes cold, and his appetite vanishes. The cause of all these phenomena is the withdrawal of the natural heat and blood into the body. The reverse of this is seen in an individual of weak physique, changeable color, and tender voice, as soon as he is met with something that rejoices him a great deal, how his physical strength is increased, his voice raised, the face lit up, his movements become lighter. His pulse beat becomes stronger, his body surface warmer, joy and delight appear so evident that he no longer can conceal it and keep it to himself. All these happenings, the movements of the natural heat and the blood to the periphery of the body, the condition of the body, and the condition of the coward and hopeful as well as that of the indifferent and phlegmatic person are well known, and likewise the conditions of the one in despair as well as of the one conscious of success are clear."

(From a translation by Harry A. Savitz, M.D., in *Annals of Medical History*, 1932, iv, 80-86.)

A Sporadic Benign Rickettsial Fever With Occasional Exanthem

By Noxon Toomey, M.D., F.A.C.P., *Palmyra, Missouri*

IN the north temperate latitude, fevers of abrupt onset and intense, short course, but without rash or contagiousness are among the commoner ailments of the summer months. Food or water borne infections cause a goodly proportion of such cases. The respiratory tract infections, exacerbations of chronic intestinal, nasopharyngeal or other focal infections, and the acute pyogenic processes of cryptic location all contribute such a share of cases that by coincidence and concatenation of circumstances they may even give rise at times to the false appearance of a sporadic or epidemic disease being present in a locality. Acute non-exanthematic infections of transmissible nature, such as mild anterior poliomyelitis in sporadic or epidemic form, influenza and other known diseases, such as scarlatina in a very mild form, may also cause a sporadic outbreak the nature of which is not recognized at first, or even throughout its course, provided necessary diagnostic procedures are not carried out.

That the food and water borne infections, endogenous and contact diseases do not, however, account for all sporadic outbreaks in the summer months of the north temperate latitude may be suspected from our knowledge of the insect borne diseases, such as malaria, typhus fever and dengue of the less temperate climates. It is possible, therefore, that insects are the vectors of some of the acute, prostrating, non-exanthematous fevers of short duration and unknown nature, as observed in the north during the summer months, and called "summer flu" or summer influenza. Whether this sporadic summer disease of the north is in reality influenza or an influenza-like disease, or some quite distinct sort of disease has not been investigated at all, it having been taken too generally for granted that it is "influenza for all practical purposes". While one cannot deny that influenza may occur epidemically, or even sporadically, in the summer months, yet it actually appears that most of the cases of so-called "summer flu" have characteristics by which a careful observer can distinguish them from influenza as it is known in the winter and spring, and in reality throughout the whole year.

The main clinical differences between influenza and the so-called "summer flu" consist in the absence in the latter of lacrymation, coryza (or rhinorrhea) and more or less bron-

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chitis, whereas in "summer flu" the fever is higher and steadier, the pulse more rapid and wiry, and in "summer flu" there is greater likelihood of nausea, vomiting and constipation, but less hebetude and drowsiness, the initially keyed-up sensorium of "summer flu" giving place at times to a light delirium. While headache, backache and aches generally are equally common in both diseases, the weariness and malaise of influenza are comparatively more vaguely localized; whereas in "summer flu" they are more apt to be described as neuralgic or rheumatoid pains in definite places, chiefly the neck, back and extremities. One curious minor difference is that the neuralgia of the scalp so commonly encountered in influenza is absent in "summer flu". Finally it may be said, but with less assurance, that the convalescence from "summer flu" is more rapid than from influenza; at least it does not have a sequential nasopharyngeal suppuration as influenza may have.

Surmising from the above facts that "summer flu" may consist in part, at least, of some disease of unknown nature, it has been our object to determine the nature of the disease, its mode of spread, and in whatwise it may be a form of, or else related to, well known diseases that occur elsewhere, particularly in less temperate climates.

The data and conclusions presented herewith are the result of observations extending over a period of six years, and are a development of certain early observations that suggested but did not at once prove that certain spotted and typhus-like fevers might follow the bites of certain blood sucking bugs (hemiptera). A discussion of the cases with exanthem conforming to the spotted fever type or the endemic typhus type, with particular reference to the vectors involved, will be reserved for a subsequent paper. This article will be limited, therefore, to a description of the non-exanthematic, or very usually non-exanthematic fever, that has, in the northern states, added its cases to the medley popularly known as "summer flu". For the sake of preciseness and clarity, the basis for our characterization of this definite entity will be the following presentation of our findings in a definite group of cases studied recently. We were led to investigate this sporadic outbreak on account of our interest in, and in conformity with, conclusions that we had previously deduced from a study of cases in which the element of sporadic outbreak was not so well marked. In general it may be said, however, that our previously recognized isolated cases conformed in clinical course to the disease here described as a typhus-like disease, and that a consideration of them would not alter or add to the characterization of the disease as made out from a study of the sporadic group upon which we base our report, except insofar as to indicate that the non-exanthematic typhus-like disease of the summer months in a temperate climate may occur as isolated cases and may run a somewhat milder course than encountered for the most part in the sporadic outbreak reported in this article.

A systematic description of the disease will be followed by epidemiologi-

cal notes on the sporadic outbreak that was the source of this material, by case histories of ten of the eleven cases in this group, and by protocols of blood studies on eight of the above mentioned eleven cases. A comparison with the related diseases of the typhus-spotted group will conclude the article.

Description of the Benign Typhus-like Disease

Initial bites by insects have been noted in about 80% of the cases. The lesions at the sites of the bites have been small erythematous papules about three millimeters in diameter. The papules have never ulcerated nor commonly shown vesiculation at their apices.

The incubation period varies from ten to fourteen days, being mostly twelve days in duration. Well characterized prodromes do not occur, although a fourth or a third part of those about to take ill notice an unusual sense of fatigue, and a vague malaise for some hours before onset.

Without a preceding subnormal temperature, the onset comes on suddenly (or occasionally subabruptly) with nausea, malaise and a rapid accession of fever. With the rise of the latter there may be a feeling of chilliness, but this is not an outstanding feature of the onset. Rigors occur only very exceptionally. Dull headache, chiefly of a diffuse or vertex type, is complained of by patients during or a little after the onset. Abdominal discomfort, rarely severe, and usually of upper abdominal or diffuse type, develops *pari passu* with nausea and vomiting. The latter usually occurs one or more times, and often repeatedly, protractedly, and with bilious ejecta.

Neuralgic or rheumatoid pains are not a prominent feature of the disease at onset or latterly, but occur to some extent, being noticed in the cervical and dorsolumbar muscles chiefly, and as cramp-like pains of the extremities, chiefly the lower.

The fever reaches a fastigium (or prefastigium) of 104°F. to 105°F. within twelve hours, usually rising during the next twenty-four hours (with or without a slight preceding remission) to a perfastigium of 105.5°F. to 106°F. The latter temperature, or more usually a degree lower is held with very slight remissions for the next sixty to seventy-two hours thereupon declining by very rapid lysis to normal or near normal, or even subnormal. Sometimes the lysis is not so rapid, the temperature declining consistently at the rate of about two degrees a day for two or three days. A secondary rise will be noticed later.

Both pulse rate and respirations are accelerated, the latter in proportion to the fever, but the pulse, up to 140 or 145 per minute, being for the most part slightly accelerated out of proportion to the temperature; although well sustained, tense and wiry, except in elderly persons.

Toward the end of the first twelve or eighteen hours of fever the face becomes flushed and the conjunctivae become intensely congested, but lacrymation, rhinorrhea, coryza, or turbinal or pharyngeal congestion do not occur at any time. Faucial or tonsillar engorgement is invariably absent, and a subjective sensation of sore throat is

almost never noticed. Cough is infrequent and invariably dry, but most patient cough a little toward the end of the disease.

Constipation is troublesome from the outstart, and throughout the whole course of the disease, often falling but little short of a serious obstipation. The tongue becomes coated with a universal, thin, dry, white fur, but is neither swollen nor shrunken, nor protrudable with difficulty. There is no difficulty in micturation.

The sensorium is clear throughout the first two or three days, sleep being usually troubled, and occasionally somewhat wanting. Delirium, even the mildest, is a quite exceptional occurrence, but has been noticed for brief periods in a few cases. Micropsia was reported in one case. Drowsiness supervenes after the first two or three days (occasionally earlier) but stupor does not occur. Increase of mental and muscular fatigability are noticed toward the end of the disease, but with onset of convalescence the mental and muscular tone improve rapidly, even at a rate greater than the impaired circulatory tone would seem to justify. The moderately impaired circulatory tone and the considerable secondary anemia are the chief features of the latter course of the disease. The appetite returns readily.

A rash is not a frequent phenomenon of the sporadic benign rickettsial disease. It occurred once only in the eleven cases of this epidemic. Premonitory phenomena such as marmoraceous mottling, erythema of the skin, etc., do not occur except that the face is almost habitually flushed after the fever reaches the height of its initial ascent.

The rash as observed consisted of a lentil sized, non-confluent, erythematomacular (deep rose colored) exanthem that appeared three and a half days after onset and was at no time either hemorrhagic or pruritic. It appeared first around the ankles and thence spread up the lower limbs to reach the groins by the end of the first day. The arms broke out not quite a day after the first appearance of the rash; the abdomen, flanks and chest, in order named, being the last parts to become involved. The rash faded quickly with the subsidence of the fever, but came out again less intensely during the secondary rise of the temperature.

A secondary rise of temperature was observed as an unmistakable phenomenon in one-half of the cases, but could be noticed to a slight degree in most of the other cases. In most instances the remission fell to below normal and lasted only a day or a little less, but in one case the remission lasted two days. The secondary rise lasted only one day, and seldom exceeded 101°F. Subsequent remissions of very slight degree were noticed in one or two cases.

In four cases, a blanching of the papules at the site of insect bites was noticed two to four days following the lysis of the fever. It was quite probable that this phenomenon occurred in other cases but failed to be observed. The white spots of the anemic areas lasted two to several days.

Epidemography

In early August of 1932, there occurred in Pittsfield, Illinois, the almost simultaneous appearance of eleven cases of an acute (mostly) non-exan-

thematous, hyperpyrexial fever of short duration. The known cases of clinically distinguishable character occurred chiefly among a party of boys who visited a natural swimming pool. The latter had long been a resort known favorably for its sanitary character.

On the day of exposure, July 26, the pool was visited by two groups, the boys above mentioned, and a smaller group that did not partake of the same food as the boys, and kept well apart, although not strictly isolated from them. Nine cases developed among twenty-three persons (three adults and twenty children) comprising the boys' group, and one (possibly two) cases developed among five adults and four children comprising the other group. The following day the pool was visited by a small group in nowise in contact with either of the first two groups. In this third group one case developed.

Food could be positively excluded as the source of the infection inasmuch as all twenty-three persons of the first group partook of the same food, but only nine were taken ill. The food consisted of peanut butter and pimento sandwiches, homemade cookies, deviled eggs, and ice cream cones. No water was drunk at the pool or at a farmstead as the meal was eaten in town.

Water of the pool swallowed by the boys while in swimming could not so clearly be excluded as the source of the infection. This possible source was considered the more likely on account of the pool being more turbid than usual due to a preceding rain that had washed the surrounding drainage area, mostly orchard lands. However, of the thirty odd persons who were in swimming, only ten became ill. On the other hand, one adult (case C. C.) who became infected was known not to have been in or close to the pool. The boys changed clothes at various places behind a thicket of small trees and bushes. It was not possible to correlate the cases with any particular place in the brush. No one encountered a living or dead rodent in or near the pool. Insect bites were experienced by many who visited the pool, and by all who took ill, but only one patient (case C. C.) was able to identify at least one species of insect; these she identified as hymenoptera of the genus, *Halictus*, popularly known as "sweat bees". The latter fact was corroborated by another adult who was stung by sweat bees and possibly had a mild attack of the disease, but whose case was not investigated serologically, and was not included in this series. Whether fleas also were present or absent was not determined, but they were known to be a common pest elsewhere about the countryside at that time. With a high degree of probability it was possible to exclude ticks, blood-sucking bugs (hemiptera) and mites (chiggers) as the actual vector.

That the disease was not caused by a typhoid or paratyphoid organism was evident from the negative findings (by agglutination and culture) made on blood and stool specimens sent from several of the cases to the Illinois State Board of Health Laboratory, Springfield, Illinois.

Case Histories

Case I. H. U. (Case of Dr. Frank N. Wells). A tall, spare built lad of 14 years

of age. He had been quite well for the preceding several years. Without prodromes, he became suddenly ill on the evening of Friday, August 5, the onset being characterized by headache, lassitude, malaise, broken slumber, and coldness such as led him to keep under heavy bed covers on a hot day; but chill and rigors were absent. His temperature at noon the next day was 102.5°F., rising steadily to 105°F. by that evening. Thereafter, for forty-eight hours the fever continued constantly at 104° to 104.4°F, except for brief periods following spontaneous hyperhidrosis, when it fell to 102.5° or 103°F. Drenching sweats, occurring every three or four hours, were a feature of this case from shortly after onset until after defervescence. Sleep occurred only for brief periods following the sweats, and was troubled with frightful dreams. Between naps there was no drowsiness or delirium, the sensorium being clear but without ability to concentrate.

By the end of the first 24 hours the face was flushed and the eyes became "terribly blood shot—shot with red—and sore in their sockets, but the eyes did not run; there was no sore throat at any time". Headache persisted from onset, but nausea did not develop at once, the patient vomiting for the first time about 48 hours after onset. Vomiting persisted for three days, possibly due partly to exhibition of calomel. The temperature was kept to 104°F. the third (Monday) night by constant allover cool sponging, the pulse then being 110 to 116, but cyanosis such as could be recognized by a layman was not present.

Three and one-half days after onset the boy broke out with a nonpruritic, macular, nonhemorrhagic rash of splotchy appearance and deep rose color, that first appeared around his ankles and spread upwards throughout the day. His arms broke out Wednesday morning, and the abdomen and chest during the afternoon of the same day. Twelve hours later the rash faded quickly with subsidence of the fever, but returned faintly that evening with a return of the fever. The bowels were extremely constipated from onset throughout the course of the disease, and when they were finally moved the dejecta had an unbearable odor. Dysuria was never present.

Case II. R. N. (Case of Dr. Wells). A nine year old boy; previously healthy. He experienced no prodromes. The onset was sudden and violent Saturday morning, August 6. The onset was characterized by nausea and terrible headache, with rise of temperature to 102° F. (at 8 A.M.), and a slight feeling of chilliness but no chill. Nausea and headache persisted throughout the day, a stiff neck, without local tenderness or cervical adenopathy supervening. The temperature rose to 103.6° F. (6 P.M.) the face becoming flushed, and the conjunctivae intensely congested, but sneezing or rhinorrhea were at no time in evidence. That night the boy did not sleep; the fever rose to 104.5° F.; he vomited the next morning. For two and one-half days the patient was "bordering on delirium", with a constant temperature of 105° F., reaching 106.4° (axillary) at 4 P.M. Wednesday, but falling by the early part of next day. Hyperhidrosis was not a pronounced feature. A right inguinal adenopathy was noticed during the early course of the disease. After the fifth day a dry hacking cough, "but nothing of pronounced degree" occurred for three days.

The pulse was slow, weak and intermittent throughout Friday and Saturday, the seventh and eighth days of the disease. A stubborn constipation, noticed shortly after onset, persisted throughout the disease. A secondary rise of temperature, to 102° F. occurred on the seventh day. No rash had appeared at any time, but on the eleventh day it was observed that the previously noticed "bites" had become minute hard papules and totally anemic (intensely white) in color.

Case III. R. Mc.R. (Case of Dr. McRaven). A 10 year old boy with a history of having had two or three prior attacks of abdominal distress, but none for the preceding eight months. He became suddenly ill Sunday evening, August 7, with chilliness (but no chill), languor, and a rapid rise of temperature. He had no abdominal tenderness or vomiting at onset. His fever maintained between 105.4° and 105.6°F. for three days and then fell by rapid lysis to near

normal. While the fever was high his face was flushed, his conjunctivae were congested and his bowels were constipated, but he was without lacrymation, coryza, sore throat or bronchitis. He had no rash, and his sensorium remained clear.

Abdominal tenderness and vomiting supervened after the second day of fever, and again during the secondary rise of his fever, but as the latter attack appeared to be a recrudescence of his previous appendiceal trouble, he was hospitalized and no longer considered an uncomplicated medical case.

Case IV. L. G. (Case of Dr. Peacock). An 11 year old boy, not previously ill. He had a prodromal malaise for some ten hours before onset. Onset was Saturday evening, August 6, with headache, stomachache and rise of temperature to 102.5° F. He did not vomit at onset or at any time afterwards, although his head ached almost constantly throughout the course of disease, and stomach ached from time to time. After the first twelve hours the temperature rose to 104.5° F. and continued thereabouts constantly for three days, reaching 105°F. in the evening of the fourth day, and thence twelve hours later declined by a rapid lysis. Shortly after onset his eyes became blood shot and his condition progressed to what was called a dry granulation of his lids, with photophobia but without a mucoid or purulent exudate. His throat at no time became injected or sore although he had a slight cough towards the end of the fever. His doctor thought he heard some fine râles in the upper part of chest. Constipation was not a marked feature; diarrhea did not develop. There was no lymphadenopathy. Following the lysis there were two or three remittances of the fever, but accurate records were not kept. No rash developed. Insect bites, believed to be mosquito bites, had been noticed.

Case V. D. L. (Case of Dr. McRaven). An anemic boy of small stature for his age of 13 years. Some two to three weeks prior to his illness, his father had a short, prostrating fever with violent rigors and nausea but no sore throat, coryza, bronchitis or exanthem. His mother and sister were likewise ill shortly afterwards, but only moderately to slightly so.

The boy became ill suddenly, Saturday night, August 6, with headache, prostration and a sudden rise of temperature to 103° F. He did not vomit until the next morning. "His eyes became terribly blood shot and his nose ran although his throat was clear and not sore at any time. For three days and three nights his fever was 103°F. and did not vary the least at any time. He developed a pain behind his ears and aches down his legs. His bowels scarcely moved at all and never got loose. About the fourth day his nose began to run, his eyes watered, and he developed a dry cough, after which he spat up a lot for a day or two. His headache, which had gone away, came back terribly with the return of the fever." This patient had an abrupt lysis on the fourth day with intermittence of one day, and a secondary rise on the sixth. His sensorium remained clear, and no rash developed. Ten or eleven days after onset, his mother found noticeable for the first time, white macules about 3.5 mm. in diameter. These were scattered at random over the upper part of his chest, shoulders and neck. On at least one, and probably two occasions, a week or so after defervescence, and following moderate exertion, he had a sharp rise of temperature lasting several hours.

Case VI. W. K. (Case of Dr. McRaven). A robust boy 12 years of age; not previously ill. Onset was abrupt Saturday night, August 6, with slight malaise and chilliness, but without rigor or headache. He did not vomit until the next morning (temperature then 103.4° F.). The temperature taken Monday morning, when he again vomited, was 102° F.; it was 103° that afternoon, and 104.8° that evening. He had considerable injection of the conjunctivae (second and third days only) but had no lacrymation, coryza or sore throat. This patient had no headache or pains at any time, and no cough at any time. He was constipated throughout the whole course of the disease. There was a lysis to subnormal (98.2°) about the middle of the fifth day, and thence a slight rise (to 99.6°) twelve hours later, the temperature remaining normal after the sixth day.

Case VII. L. N. (Case of Dr. Wells). A boy thirteen years of age who had not previously been ill, was taken ill suddenly

on Sunday morning, August 7, the onset being characterized by dizziness, headache, nausea, and a rise of temperature to 102° F. He vomited shortly after onset and retched frequently and severely until the end of the third day, his temperature during the time rising to 104.4° F. at 12 hours after onset, and thereafter remaining practically constant until the end of the fourth day. After a rapid lysis, and an intermission of one day (at 99.6° F.), there was a rise to 103° F. by the end of the following day, the temperature declining to subnormal (97° F.) at the end of seventh day, but after the eighth day remaining nearly normal.

Towards the end of the fever this patient noticed some stiffness of his lower limbs. A nonproductive conjunctivitis was present, and the tongue was heavily coated, but there was no coryza, sorethroat, or cough. Constipation was troublesome throughout the whole course of the disease. The pulse (mostly 136 to 142) was unusually rapid for the temperature, according to his mother, a trained nurse. Continuous drowsiness was a feature of this case.

On the ninth or tenth day after onset, the temperature then being normal, numerous anemic macules (white spots) were noticed for the first time on the upper part of his trunk. They were where small erythematous papules, 'insect bites', had been.

Case VIII. E. A. (Case of Dr. McRaven). An active lad, 12½ years of age; not previously ill. He became ill sometime Monday, August 8, there having been for some hours what might have been a prodromal period. The latter was characterized by an extreme sense of fatigue and weariness. Onset was with headache, flushed face, conjunctival engorgement, increased malaise, and a rise of temperature to 103° F. Chilliness and vomiting did not occur and nausea was at no time in evidence. Herpes labialis was noticed on the third day, but never was his throat sore. He never coughed, nor had lacrymation or coryza. The fever reached 104° F. about 36 hours after onset, and continued (with decline to 102° F. once during the night) through the next day, receding to 103° F. and then dropping to subnormal (97.6° F.) where it remained throughout the fifth and sixth days. There was a secondary rise (to 100.2° F.) throughout the seventh day. Constipation occurred; with diarrhea at no time. The patient's sensorium remained clear. No rash developed. There was no remembrance of bone, joint or muscle pains, except for general "tiredness".

Case IX. J. C. (Case of Dr. McRaven). A somewhat nervous lad of 11 years of age, not previously ill. He became ill rather suddenly on Monday evening, August 8. Onset was characterized chiefly by vertigo, sleeplessness and rise of temperature to 101° F., there being but slight chilliness. The next morning his "face and eyes looked real red and feverish, but his eyes did not water". During the day his temperature rose constantly, reaching 104.2° F., about 24 hours after onset. Twinges of sharp pain were noticed about that time and afterwards. He did not vomit at onset or during the first few days. He was constipated, the forced dejecta being dark green and black, and very offensive; a coated tongue was noted.

His temperature continued about constant at 103.6° F., during the second, third and fourth days; the general sweat, 48 hours after onset, and several slighter ones somewhat reducing it transitorily. There was no sore throat, coryza or chest symptoms at any time. A drop of his temperature to normal through the fifth day was followed by a rise to 100° F. throughout the sixth day, exacerbation being accompanied by headache and vomiting. No rash appeared.

Case X was in a boy who visited the swimming pool about twenty-four hours after the day most of the boys were infected; and who at no time had been in contact with any one else who contracted the disease, or had partaken of food in common with them. The disease in this case was reported to have consisted of high continued fever with marked prostration, vomiting, and absence of respiratory tract symptoms and intestinal looseness. Although the disease was of the more severe sort, no rash developed. The incubation period was eleven days. Further information was not obtainable.

Case XI. Mrs. C. C. This patient was a women, 48 years of age, who had had a pelvic disorder for which an abdominal section

was done two years previously. She was not robust but had been free from abdominal discomfort and febrile reaction during the preceding twelve months. She was seized Tuesday morning, Aug. 9, with sudden profound weakness, chilliness, and general malaise, but without headache, rigor or definite nausea. Bites by insects (to a considerable extent) were sustained July 26. No conjunctivitis, coryza, sore throat, or chest symptoms developed at any time. Constipation was natural to her and was not replaced by any looseness. Diffuse abdominal soreness, without nausea, but with pains in the sides and the back, was a prominent feature of this case. Frequent heavy sweats at irregular intervals and profound drowsiness, both of which lasted five or six days, were outstanding features. A temperature record was not preserved, but it was clear that after an illness of eight days she quite suddenly improved, and for the following weeks remained free from symptoms suggesting a focal infection. Although a definite retrospective diagnosis was not possible in this case, the apparent occurrence of an incubation period, the sudden onset of a severely prostrating illness with numerous irregular sweats, the absence of symptoms suggesting one of the commoner focal ailments, and the sudden convalescence after eight days suggested that she may have had the benign typhus-like disease (a fact later confirmed serologically).

Blood Morphology

No blood counts were made by the attending physicians during the early course and fastigium of the disease. While the blood picture as found by the author at the end of lysis, and recorded below, is not conclusive evidence of a particular type of reaction, nevertheless it is evident that the disease produced a secondary anemia of moderate degree, and a slight leucocytosis, the latter being due chiefly to an absolute and relative increase in the lymphocytes and mononuclears, a change almost invariably noted in the rickettsial group of diseases.

Table I

Blood Counts Toward End of the Disease

Case	Age of Patient	Day of Disease	W.B.C. Count	R.B.C. Count	Hemoglobin	Index Corrected for Age Norms	Other Formed Elements
I. H. U.	14	9.5	8,100	5,200,000	55%	0.70	Platelets +
II. R. N.	9	9	8,550		60%		Platelets ++
V. D. L.	13	9	9,000	5,100,000	55%	0.70	Platelets ++
VI. W. K.	12	8	10,000	5,250,000	70%	0.90	Normal
VII. L. N.	13	8	8,700	5,320,000	65%	0.80	Platelets ++
VIII. E. A.	12.5	8	9,100	5,200,000	60%	0.75	Dust increased
Average	12.3	8.6	8,900	5,214,000	61%	0.77	Platelets +

Table II

Differential Counts

Case	Age of Patient	Day of Disease	Bas.	Eos.	My.	J.	St.	Segs.	Lymphs.	Monos.	Trans.
I. H. U.	14	9.5	0.0	1.4	0	0	1.0	43.1	47.7	6.	0.9
II. R. N.	9	9.	0.7	7.0	0	0	0.7	45.	40.	5.	
V. D. L.	13	9.	0.0	2.2	0	0	1.4	37.	50.	9.	0.4
VI. W. K.	12	8.	0.0	2.4	0	0	1.6	51.	40.	5.	0.0
VII. L. N.	13	8.	0.5	2.5	0	0	1.5	45.	38.	12.	0.5
VIII. E. A.	12.5	8.	0.4	2.6	0	0	1.0	37.	47.	12.	
Average	12.3	8.6	0.3	3.0	0	0	1.2	43.	43.8	8.	

Serology

Specimens of six sera were titrated against two local strains of *Proteus* of unknown type, but for the purpose of this article known as M_1 and M_2. While our titrations against these strains gave fairly significant results it was thought best to ask that titrations be made against a large number of strains of Proteus X organisms. Accordingly, six samples of the sera were sent to the National Institute of Health, Washington, D. C., and six samples to the Rocky Mountain Spotted Fever Laboratory, Hamilton, Montana. In each instance it was asked that the sera be titrated against the following strains of *Proteus X:* OXK, HXK, OX_2, OX_{19}, HX_{19}, W (N.H.I. No. 533), 271, 560, and 568.

In reply to our request, Dr. R. E. Dyer, Acting Director of the National Institute of Health wrote under date of August 22, 1932, as follows:

"These serums have been run against *B. proteus* X_{19}—No. 504, which our experience has shown to be the most sensitive of our stock cultures of *B. proteus.* The result as shown on the enclosed sheet are suggestive that the cases are either typhus or mild spotted fever, and we would suggest since these samples were taken about the 8th or 9th day of fever, second samples be withdrawn sometime after the end of the second week. They may show a much higher titer."

Titrations at the National Institute of Health were made against only B. proteus OX_{19}— No. 504. The protocol of these titrations is as follows:

Table III
Titrations against Proteus OX_{19}—No. 504

	Case	Days after onset	N.H.I. No.	1/20	1/40	1/80	1/160	1/320	1/640
I.	H. U.	9.5	3248	4	4	2	0	0	0
II.	R. N.	9.	3247	4	4	2	0	0	0
V.	D. L.	9.	3249	4	4	4	4	2	0
VI.	W. K.	8.	3251	4	4	0	0	0	0
VII.	L. N.	8.		4	4	4	4	2	0
VIII.	E. A.	8.	3250	4	4	4	4	0	0

To determine whether there was an increase in the titer during convalescence, the following specimens of blood drawn 18 to 20.5 days after onset (or about 9 to 10 days after defervescence) were titrated against strain No. 504 with the following results:

	Case	Days after onset	1/20	1/40	1/80	1/160	1/320	1/640
II.	R. N.	20.5	4	4	4	2	2	0
V.	D. L.	20.	4	4	0	0	0	0
VII.	L. N.	19.5	0	0	0	0	0	0
VIII.	E. A.	19.	4	4	4	0	0	0
IX.	J. C.*	18.5	0	0	0	0	0	0
XI.	C. C.*	18.	4	4	2	0	0	0

*No prior specimen submitted.

The protocol of the titrations made at the Rocky Mountain Spotted Fever Laboratory is as follows:

TABLE IV

AGGLUTINATION TITERS FOR PROTEUS X STRAINS—LIVE ANTIGENS

CASE	AGE OF PATIENT	DAYS AFTER ONSET	OX_{19}—No. 504 1/20	1/40	1/80	1/160	OX_{19} No. 271 1/20	1/40	OX_{19} No. 560 1/20	1/40	OX_{19}—No. 1 1/20	1/40	1/80
I. H. U.	14	9.5	4	2	0	0					2	0	0
II. R. N.	9	9.	0	0	0	0					0	0	0
V. D. L.	13	9.	4	4	4	2					4	4	2
VI. W. K.	12	8.	4	4	2	0	4	2	4	2			
VII. L. N.	13	8.	2	0	0	0					0	0	0

KINGSBURY STRAINS

		OXK 1/10	1/20	1/40	1/80	HXK 1/20	1/40	1/80	HW 1/20	1/40	OX_{19}—No. 2 1/20	1/40	1/80	1/160
I. H. U.						4	2	0	2	0	2	0	0	0
V. D. L.			4	4	2	4	4	2			4	4	4	2
D. L.*			2	0	0	2	0	0						
VI. W. K.						4	2	0	4	0				
VII. L. N.			4	2	0						2	0	0	0
VIII. E. A.*	2		0	0	0									

*National Institute of Health

Eight to nine days after onset, none of the cases agglutinated the X_2 strains. However, blood drawn eleven days later, from cases II, V, VII, VIII, and XI, showed a very low and incomplete titer for both HX_2 and OX_2.

Comments of Dr. R. R. Parker, Special Expert in charge of the Rocky Mountain Spotted Fever Laboratory, under date of August 26, 1932, were as follows:

"As a result of our experience with this agglutination test in Rocky Mountain spotted fever, I would be inclined to feel that these results mean little, either in a negative or positive way. Identical results with those listed could be secured with perfectly good clinical cases of Rocky Mountain spotted fever. We could also secure as high agglutinin titer as the highest shown in your series with the sera of occasional persons whom there is no reason to suspect have ever had a typhus-like infection. I offer these comments for whatever you may think them worth.

"The result of possible significance in connection with these tests is that the sera of Underwood, Kern, Logsdon, and Niebur all show some agglutination of the Kingsbury strains, either OXK, HXK, or both. The agglutinin titer is, of course, very low, but in our experience it is very seldom that either a normal or a spotted fever serum causes agglutination of this strain even at 1:10. As possibly you may know from the literature, there are certain of the typhus-like infections that agglutinate Kingsbury strains more consistently than any other *Proteus X* organism.

"Certainly one has to admit that the possibilities of transmission of typhus-like diseases by biting insects have only been touched."

Concerning an increase in titer of sera drawn from four cases (cases II, V, VII, VIII) on the eighteenth to nineteenth day after onset, Dr. Parker, under date of Sept. 22 1932, wrote as follows:

"I am forwarding the results of the agglutination tests with the second group of six sera. It appears difficult to draw any definite conclusions from these results. Possibly the most suggestive data are those for the Richard Niebur case, in which all three

proteus strains used for the first test and found negative showed low agglutination for the sample of Sept. 7. The two samples for Logsdon show no essential difference. The second sample for Louis Niebur shows a slightly increased titer against two strains. These are the same two strains that showed increased titer in the second sample from Richard Niebur. This may be of some significance."

Animal Inoculations

Seven healthy guinea pigs weighing from 236 to 810 grams were inoculated, each with one blood specimen from one of the cases indicated in the accompanying protocol. The blood was injected intraperitoneally after the abdomen had been shaved and wiped with merthiolate 1-1000. In several instances a minute amount of the blood specimen was injected into the cornea of one eye.

Concerning what may be regarded as a febrile reaction in guinea pigs it has been our experience that a normal *average* temperature for pigs of the ages used in our experiments, and kept under optimum housing and nutritional conditions at a room temperature of 80° F. (26.7° C.), may be determined as being approximately 102.4° F. (39.1° C.) with maximum *average* variations from 101.5° F. (38.6° C.) before morning feeding, to 102.6° F. (39.2° C.) after afternoon feeding; younger pigs usually having a slightly higher temperature than older pigs. In individual cases the range of normal is from 100.8° F. (38.2° C.) to 103.6° F. (39.8° C.) Hence in testing out individual pigs a temperature up to 103.6° F. should be considered within the range of normal. When, however, the temperatures of a number of guinea pigs submitted to a group experiment are taken at the same time and averaged together for the purpose of constructing a histogram of the average temperature, it seems proper to compare the ascertained average with the known normal average under the prevailing housing and nutritional conditions. It is on that basis, therefore, that the following graph (see chart II) has been prepared. For the daily temperature readings of the individual guinea pigs see table IX.

Towards determining whether the virus causative of these cases was that of typhus fever or spotted fever, or possibly a yet unidentified typhus-like virus, it became necessary to determine whether the disease produced in the guinea pigs by the unknown virus left them susceptible to or wholly or partially immune to test viruses of known character: those of spotted fever and of typhus fever. Accordingly, blood virus of known character was inoculated as indicated in table VII. This table is a consolidation of observations

Table V

Results of Guinea Pig Inoculations

	Case	Number (weight of) guinea pig	Amount of blood injected	Approximate amount per kilo	Days after onset of disease	Results* Max. temp.	Day
I.	H. U.	570 (gms.)	0.4 c.c.	0.71 c.c.	9.5	Positive (104.9°	7th)
II.	R. N.	810	0.7 c.c.	0.86 c.c.	9.	Positive (105.4°	7th)
V.	D. L.	885	1.8 c.c.	2.00 c.c.	9.	Positive (105.1°	7th)
VI.	W. K.	705	1.8 c.c.	2.50 c.c.	8.	Positive (105.0°	7th)
	Inoculated Two Days Later with Proportionately More Erythrocytes						
II.	R. N.	236	0.65 c.c.	3.00 c.c.	9	Negative	
VII.	L. N.	240	1.15 c.c.	4.75 c.c.	8.	Negative	
VIII.	E. A.	750	3.00 c.c.	4.00 c.c.	8.	Positive (105.6°	5th)

*For daily temperature readings of guinea pigs see table No. X, items 1 to 7 inclusive.

made independently by the author, and by Dr. R. R. Parker at the Rocky Mountain Spotted Fever Laboratory. Dr. Parker kindly furnished us with Rocky Mountain spotted fever blood virus to make our tests, but as there was the possibility of the spotted fever losing potency in transit, we shipped four of our guinea pigs to Dr. Parker, who kindly carried out cross-inoculation tests on them. Similarly, five of our pigs infected with the unknown virus, after we tested them against spotted fever virus, were shipped to Dr. R. E. Dyer, Acting Director, National Institute of Health, Washington, D. C., where they were cross-inoculated with typhus. The protocols of the cross-immunity tests are set forth in tables VII and VIII.

To determine whether persons convalescent from the benign rickettsial fever still carried the live virus in their blood, six guinea pigs were inoculated, each with the fresh whole, non-citrated blood of one case drawn on the eighteenth to twentieth day after onset. The results are set forth in table IX.

Comparative Pathology

Numerous typhus,[2,17,22] typhus-like,[4,15,23,28] and spotted fevers,[12,19,20,26] of diverse types have been described in recent years. Lately these fevers have been arranged systematically according to their serologic reactions, their clinical manifestations, and the biologic positions of the vectors involved in their transmission.[31] On that account it is now inadequate to give a clinical description of a typhus-like disease without accompanying the report with

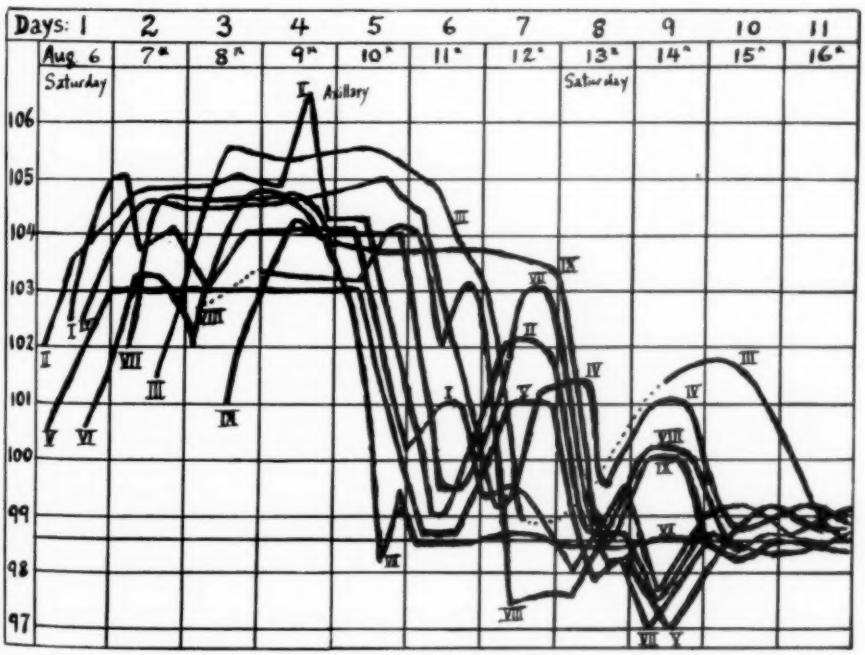

Chart I
Temperature Curves of Nine Cases

TABLE VI

DEMONSTRATIONS OF RICKETTSIAL ORGANISMS

	CASE	GUINEA PIG NO.	SEX	SMEAR FROM TESTICLE	PERITONEAL SCRAPING	CORNEAL PUNCTURE	SECTION OF BRAIN
I.	H. U.	570	F	Not made	Not made	Grossly negative	Not made
II.	R. N.	810	M	Not made	Not made	Grossly negative	Not made
II.	R. N.	595	M	Positive	Positive	Not made	Positive
V.	D. L.	885	F	Not made	Not made	Grossly negative	Not made
VI.	W. K.	705	F	Not made	Positive	Microscop. positive	Positive
VII.	L. N.	666	M	Positive	Not made	Not made	Not made
XI.	C. C.	732	M	Positive	Positive	Not made	Positive

Guinea pig numbers indicate weight in grams of respective animals when first taken for experimental purposes. All guinea pigs lost from 24 per cent to 30 per cent (average 26 per cent) of their weight as a result of the typhus-like infection.

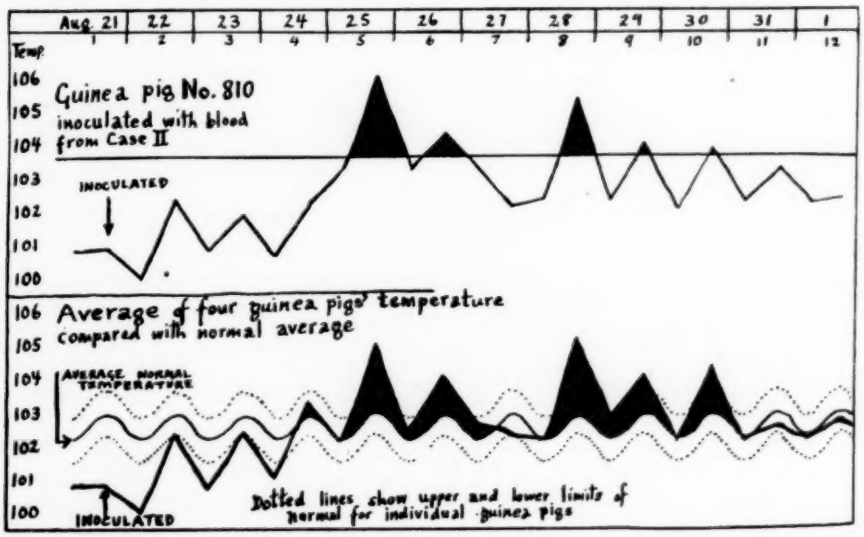

CHART II

TEMPERATURE CURVES OF THE DISEASE IN GUINEA PIGS

Upper graph represents typical temperature curve of individual guinea pig charted according to method employed by U. S. Public Health Service (recognizing as febrile only temperatures above 103.6° F.)

Lower graph represents histogram of average temperatures of four guinea pigs (Nos. 570, 810, 885, 705) each inoculated with a blood virus from one of four cases (Cases Nos. I, II, V, VI). Graph charted to indicate diurnal variation in average normal temperature of guinea pigs.

TABLE VII
CROSS-IMMUNITY TESTS AGAINST ROCKY MOUNTAIN SPOTTED FEVER

CASE	GUINEA PIG NO.	TEST MADE BY	AMT. R.M. S. F. VIRUS INOCULATED	ORIGINAL INOCULATION	RESULTS	FOR TEMP. CURVE SEE TABLE X
I. H. U.	570	Parker		9.5 day blood kept 6 days	Susceptible to R.M.S.F.*	
II. R. N.	810	Toomey	1.5 c.c.	9th day blood kept 6 days	Delayed, mild reaction to R.M.S.F.	Item 14
II. R. N.	236	Toomey	1.0 c.c.	9th day blood kept 8 days	Almost immune to R.M.S.F.	Item 15
V. D. L.	885	Toomey	1.0 c.c.	9th day blood kept 6 days	Immune to R.M.S.F.	Item 16
V. D. L.	503	Parker		Convalescent's 20th day, direct	Susceptible to R.M.S.F.*	
VII. L. N.	240	Toomey	1.0 c.c.	8th day blood kept 8 days	Delayed, mild reaction to R.M.S.F.	Item 17
VII. L. N.	666	Toomey	1.0 c.c.	Convalescent's 19.5 day, direct	Excluded account wasting disease	Item 18
VIII. E. A.	750	Parker		8th day blood kept 8 days	Susceptible to R.M.S.F.*	
IX. J. C.	381	Parker		Convalescent's 18.5 day, direct	Susceptible to R.M.S.F.*	
Controls	564	Toomey	1.0 c.c.		Positive, mild	See Item 19
	407	Toomey	1.0 c.c.		Positive, typical	Item 20
	770	Toomey	1.5 c.c.		Positive, very mild	Item 21

*Letter report by Dr. R. R. Parker, October 4, 1932.

TABLE VIII
CROSS IMMUNITY TESTS AGAINST TYPHUS FEVER

CASE	GUINEA PIG NO.	TEST MADE BY	ORIGINAL INOCULATION	RESULTS
II. R. N.	810	Dyer	9th day blood	
II. R. N.	236	Dyer	9th day blood	All survivors were susceptible to endemic typhus.*
V. D. L.	885	Dyer	9th day blood	
VII. L. N.	240	Dyer	9th day blood	
VIII. E. A.	610	Dyer	Convalescent's	

*Letter report by Dr. G. W. McCoy, Director, National Institute of Health, October 8, 1932, as follows: "The five guinea pigs received from you on September 22. have been tested for immunity to endemic typhus as you requested. Three of them gave the usual reaction of fever and redness and swelling of the scrotum and hence were considered non-immune to endemic typhus, while two of them died during the course of the test, presumably from secondary infection, and it could not be determined whether they were immune."

TABLE IX
TESTS FOR VIRULENCY OF CONVALESCENTS' WHOLE BLOOD

CASE	GUINEA PIG NO.	SEX	DAYS AFTER ONSET	AMT. OF BLOOD INJECTED	C.C. PER KILO	RESULTS*	SEE
II. R. N.	595	M	20.5	4.5	7.5	Very virulent	Table X, Item 8
V. D. L.	503	M	20.	9.1	20.0	Virulent	Table X, Item 9
VII. L. N.	666	M	19.5	5.0	7.5	Probable but uncertain	Table X, Item 10
VIII. E. A.	610	M	19.	5.0	8.2	Very mild	Table X, Item 11
IX. J. C.	381	M	18.5	4.7	12.4	Virulent	Table X, Item 12
XI. C. C.	732	M	18.5	5.5	7.5	Virulent	Table X, Item 13

*For daily temperature readings of these guinea pigs see table X.

TABLE X
TEMPERATURE READINGS OF GUINEA PIGS*

Inoculations with Unknown Virus in Blood Drawn 8th to 9th Day of Disease

ITEM	PIG NO.	DATE: AUG. 21	22	23	24	25	26	27	28	29	30	31	1
		x											
1	570	*8,8	1,22	10,22	14,30	22,48	27,38	28,25	26,49	33,42	29,39	21,27	22,22
2	810	8,9	0,24	9,18	6,26	31,60	31,43	32,22	24,54	23,40	20,38	22,32	23,24
3	885	8,8	0,24	8,25	12,37	19,44	14,37	23,21	18,51	30,42	21,39	20,20	19,24
4	705	8,8	0,26	0,21	10,34	21,50	24,42	26,23	24,50	26,36	13,37	21,23	20,26
Average		8,8	0,24	7,24	10,32	23,50	24,40	27,23	23,51	28,40	21,38	21,25	21,24
				x									
5	236			13,0	0,11	2,4	10,16	8,8	12,24	13,25	6,23	8,22	8,
6	240			14,26	0,11	5,4	14,18	10,0	10,30	14,30	17,29	14,28	13,
7	750			10,12	0,12	34,61	34,52	30,30	10,56	29,43	34,48	34,38	32,37

Tests for Virulency of Convalescent's Whole Blood

	AUG. 26	27	28	29	30	31	1	2	3	
	x									
8	595	19	26,40	42,62	48,	Dead				
9	503	25	20,23	41,51	40,36	17,40	24,41	26,43	21,41	To Dr. R. R. Parker
10	666	19	26,34	22,45	38,38	17,42	23,44	20,23	10,10	Required for R.M.S. fever cross-inoculat.
		x								
11	610	21	12,18	40,48	32,36	11,39	21,40	22,42	20,39	
12	381	26	22,26	24,54	22,42	14,40	20,41	22,42	21,40	To Dr. R. R. Parker
13	732	22	26,22	31,52	36,40	20,22	19,17	14,15	10,	Dead

Immunes to Unknown Virus Cross Inoculated with R.M.S.F. Virus

	SEPT. 2	3	4	5	6	7	8	9	10	11
14	810	27,29	15,24	20,40	11,24	20,21	22,28	21,25	21,40	37,28	22,
15	236	33,36	24,24	19,38	38,32	38,40	34,33	31,30	32,38	32,38	30,
16	885	19,10	16,20	10,34	20,22	20,22	20,22	22,27	27,30	27,24	24,
17	240	32,22	29,24	18,33	33,34	33,31	24,26	31,33	30,50	38,38	36,
18	666	10,10	11,13	3,2	0,11	2,5	2,5	4,8	5,11	6,10	7,
19	564	17,20	16,20	7,21	18,44	8,39	10,40	11,40	22,38	38,26	28,
20	407	16,20	14,26	13,7	26,21	20,40	20,37	42,60	61,62	60,59	40,36
21	770	16,34	15,22	13,39	30,24	12,30	11,31	19,36	37,39	38,26	32,37

*Pairs of numbers represent morning temperature (on left) and evening temperature (on right) of same day; days are in chronological order from left to right. Numbers are tenth-degrees above 100°; example, 35 = 103.5°F.; 0 = any temperature 100°F. or under.
x = time inoculated.

pertinent serologic and immunologic data.

As to what criteria will prove to be the ultimate means for classifying the fevers of the typhus-spotted fever group can not be previsedwith assurance, but those tests[13] that establish the immunologic relationships of these diseases will naturally be accepted as more fundamental than any of those concerning clinical appearance, the vector concerned, or the agglutinating properties of the blood with respect to the different strains of the Proteus X.[10,14,16,27] Whether the diverse agglutination characteristics of these diseases can be dependably correlated with their immunological differences can not at present be accepted with finality, although it does appear that the power to agglutinate either or both of the X_2, or the Kingsbury strains is a differentiating criterion of fundamental value.[4,9,29]

While the behavior of these viruses when inoculated into guinea pigs has been studied by several observers,[1,5,6,7,8,11,26] it appears that the febrile, peritoneal, scrotal, and perhaps cerebral reactions are conditioned as much or more by the degree (state) of virulency of the virus employed, than by its individual character. Thus scrotal lesions are common in the malignant form of Rocky Mountain spotted fever but may be absent in the mild forms of the disease. They are not common in the epidemic typhus of Europe but are common in certain of the American and Mexican strains of typhus fever;[1,6,30] although occasionally absent in those infections, and occasionally observed in the epidemic typhus of Europe.[7,30]

In comparison with the other diseases of the typhus-spotted fever group, the disease described in this report has a unique place. We remark it having a rash somewhat similar to the spotted fever of the Rocky Mountains, at least with respect to its upward progression from the ankles. Also, the disease appeared to give a partial, but apparently incomplete immunity to spotted fever. On the other hand it caused agglutination of the Kingsbury strains of Proteus HK and OK, something that Rocky Mountain spotted fever seldom does. Also there was a longer incubation period in the guinea pig and not as great a degree of scrotal reaction as one might expect in spotted fever, although in the eastern-southeastern states' strain of spotted fever, the scrotal reaction is not commonly observed. Ticks, the so-far-as-known only vectors of Rocky Mountain spotted fever could be excluded as the vectors of this disease. This fact raises the question whether the virus concerned was that of spotted fever somewhat altered by being adapted to a vector of a different biologic order.

In comparison with the diseases known to agglutinate the Kingsbury strains, the scrub typhus of Malasia, pseudotyphus of Sumatra, tsutsugamushi disease, and tick-bite fever of South Africa, we note them as usually having a primary sore, as invariably (?) having a rash, a more prolonged febrile course, and more pronounced nervous symptoms. In fact our benign sporadic disease is clinically less similar to the Kingsbury group of diseases than to endemic typhus, especially a mild endemic typhus *sine exanthem*. As to one other fever in which the Weil-Felix test has been found positive, the Port Elizabeth fever,[24] we note the latter's prevailingly low, irregular fever, the nervous symptoms and the rash; a syndrome quite distinct from that found in our disease.

When compared with the tick-borne *fièvre boutonneuse* (exanthematic fever) and the tick typhus of India, diseases somewhat resembling Rocky Mountain spotted fever, we find no resemblance to them greater than our disease has to spotted fever of the Rocky Mountains. On the other hand, of the tick-borne group we find the greatest similarity between our present disease and the (non-exanthematic) American mountain tick-fever described by us as a distinct entity about a year ago.[21,25] So close is this resemblance that it would at times be impossible to distinguish between these

diseases by clinical means alone; the main differences at most being that the American mountain tick-fever has a shorter incubation period, is usually accompanied by more aches and pains of muscles and bones and runs a slightly longer course with two or three remissions instead of one; but these clinical differences could be due to our present disease being caused by a less virulent strain of the same virus.

As to our present disease being a mild typhus *sine exanthem,* we can say that the low *Proteus* X_{19} titer, the mononuclear rather than a lymphocytic leucocytosis, the absence of scrotal lesions in guinea pigs, and the less accentuated disturbance of the nervous, circulatory and bronchial systems are against such a supposition.

Summary and Conclusions

An intensely febrile typhus-like disease of short duration was observed to cause a sharply localized group of cases in the west-central part of Illinois during early August, 1932. Of the eleven known cases, ten were without exanthem. One case developed on the fourth day a lenticular, ascending, non-hemorrhagic erythematomacular rash somewhat resembling the rash of mild Rocky Mountain spotted fever except that it disappeared suddenly with the lysis of the fever.

The disease was characterized by an incubation period of about twelve days, by sudden onset, abrupt rise of temperature (usually with headache, chilliness and vomiting) and by a high continued fever that fell by abrupt lysis after three or four days. A remission of one to two days was frequently followed by a secondary rise of temperature lasting one day. Constipation and an intense non-productive conjunctivitis (not accompanied by lacrymation) were characteristic symptoms. Coryza, pharyngeal engorgement and chest symptoms were wholly absent, except for an occasional slight dry cough towards the end of the disease. Neuralgic and rheumatoid pains were almost wholly absent, and the sensorium remained clear. Hyperhidrosis and a regional lymphadenopathy were occasionally observed, but were not constant features of the disease. There was no mortality.

The disease caused a slight leucocytosis due to a relative and absolute increase in the lymphocytes and large mononuclears, particularly the latter. Considerable secondary anemia developed, but convalescence was rapid.

Although the disease was undoubtedly insect borne, a primary sore at site of inoculation could not be made out in any case. Small erythematous papules, the sites of insect bites, were commonly observed to become anemic (white macules) following the termination of the fever. The vector was not identified but there was evidence suggesting that the virus was transmitted by a hymenopteron of the genus *Halictus* (family Halictidae).

Agglutination tests against strains of *Proteus X* organisms showed an affinity for the non-indologenic or Kingsbury strains in addition to a moderate affinity for the X_{19} strains. The X_2 strains were not significantly agglutinated. There was an inconstant and at most very slight increase in the agglutination titer during convalescence.

Guinea pigs were found moderately susceptible to the virus. The disease in guinea pigs was without a noticeable scrotal lesion and was principally neurotropic, thus resembling epidemic typhus more than certain strains of endemic typhus or Rocky Mountain spotted fever. Inoculation of convalescent guinea pigs with the virus of Rocky Mountain spotted fever showed that the guinea pigs were susceptible to the spotted fever virus but appeared to have a partial or group immunity to spotted fever.

Preliminary studies, not developed in this report, indicate that the disease occurs not uncommonly in a very mild form, and that it is the cause of some of the cases hitherto loosely called "summer flu" or influenza.

Clinically and immunologically it is necessary to recognize this disease as a separate entity. Serologically it is related to the diseases having an affinity for the non-indologenic (Kingsbury) strains of the *Proteus X* organisms. An approximate clinical similarity to the American mountain tick-fever is noted.

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An Obstinate Case of Intestinal Myiasis

By W. B. Herms, M.A., *Berkeley, California;* and Q. O. Gilbert, M.D., F.A.C.P., *Oakland, California*

BY the term *myiasis* is usually meant the invasion of organs or tissues of animals including man by the larvae of flies belonging to the order Diptera. Although there are a number of species of flies, notably the Oestridae (bots, warbles, etc.), in which this invasion is an obligatory form of parasitism there are many more species in which this is an accidental relationship, *i.e.*, the normal existence is free-living and invasion of the internal organs of higher animals is through ingestion of infested food or drink, or ingress through wounds or the natural openings (nasal and anal).

Among the more obviously free-living Diptera which have been definitely incriminated in intestinal myiasis is the cheese fly, *Piophila casei,* which deposits its eggs in old cheeses, ham, bacon, and similar fatty products. It is easy to understand how larvae of this species might be ingested but it is not so easy to understand how the larvae could continue to live for any length of time in the intestine. Yet Thebault[1] (1901) according to Riley and Johannsen[2] (1932) recovered living larvae of this species of fly from bloody excrement voided by a child. It has been shown experimentally that a dog fed on cheese containing these larvae suffered marked intestinal injury, the papillae of the small intestine having been destroyed in spots and the walls almost perforated, presumably the result of larval attack.

However, among the Diptera more commonly reported as causing intestinal myiasis are the lesser housefly, *Fannia canicularis* L., and the latrine fly, *Fannia scalaris,* F., neither of which breeds in materials which might normally be ingested in or with food, *i.e.*, their larval food is principally fecal material. Both species invade the house and, of course, might deposit eggs under stress of circumstances in decomposing vegetable matter or meat. Riley and Johannsen (*loc. cit.*) describe the symptoms caused by the invasion of these flies as vaguely resembling helminthiasis, or more specifically, "as causing vertigo, severe headache, nausea and vomiting, severe abdominal pains, and, in some instances, bloody diarrhea". Living larvae have been recovered in stools.

Our concern in the case we are about to describe is with a group of flies which have a much wider range

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of larval feeding habits, namely, the Muscoidea, including such genera as *Lucilia, Phormia,* and *Calliphora,* commonly known as the green bottle and blue bottle or blow flies, all of which deposit eggs on a wide range of materials including human food, particularly cold meat. Flies belonging to the family Sarcophagidae are especially partial to meat and are larviparous, *i.e.,* deposit living larvae. The larvae of this entire group of flies develop very rapidly under normal conditions reaching full growth usually in four or five days after which they leave the food in search of drier and protected conditions for pupation. The pupal stage is also quite brief. The entire life history from egg to winged insect requires but from 15 to 18 days under favorable conditions. All stages may be considerably prolonged under stress.

CASE REPORT (Q.O.G.)

The patient, Z. W., a female, age 38 years, was first seen on April 26, 1930. Her chief complaints were attacks of nausea, vomiting and diarrhea, nervousness and joint aches. She had lived in Texas for a number of years. For years she had had recurring attacks of diarrhea which would last for a short time. In 1928, there was a more severe attack. She was able to work from January, 1929, to October, 1929, when she quit because of nausea, vomiting and bowel distress. She was in bed about a month, then she went to southern California where a clinical diagnosis of tuberculosis of the bowel was made. She came to Oakland in the early spring of 1930, where we saw her first in April. Her past history included the ordinary children's diseases, pneumonia twice, father living, mother died of questionable tuberculosis when she (the patient) was a small child, one sister with suspected tuberculosis. In 1914 she had had her appendix removed for abdominal pain. She felt generally fairly good until about 1922. Since then there have been spells of nausea, vomiting and diarrhea. She was operated on again for some adhesions and two small tumors of the uterus. But the major sickness has been definitely worse the past two years. Recently finger joints have become sore, also knees and ankles, and she has had rather frequent colds.

The examination showed a slender woman, with the appearance of moderate anemia. General physical examination was negative except for abdominal tenderness. Gastro-intestinal x-ray examination was negative except for hypermotility and evidence of colitis. Urine was negative. Examination of the blood showed hemoglobin, 68 per cent; red blood cells, 3,776,000; white blood cells, 5,000; polymorphonuclear leucocytes, 75 per cent; small lymphocytes, 17 per cent; large lymphocytes, 6 per cent; eosinophiles, 2 per cent. Repeated stool examinations showed giardia and yeast cells, mucus, pus, a few cysts of *Endamoeba dysenteriae, Councilmania tenuis,* gram negative bacteria predominating. Repeated examination of stools showed no evidence of tubercle bacilli. The rectum showed congestion of the mucosa with rather marked internal hemorrhoids which bled easily. Five months later cysts of *Endamoeba dysenteriae* were still found. The patient had a prolonged treatment of emetine intravenously, quinoxyl, and autogenous vaccine from stool cultures. There was general improvement in the patient's condition during the summer and fall. However, there were recurring attacks of nervousness, vomiting and diarrhea and apparently rather frequent hemorrhages from the bowel. The patient was considerably depressed at times and treatment was difficult because of lack of coöperation except after she had had a bad spell. Because of the difficulty of obtaining stool specimens, especially during the acute attacks, and in view of the fact that we had felt that there must be other reasons for her condition, early in the spring of 1931 during an attack of nausea with vomiting and diarrhea we kept the patient for one entire day in the office under observation and obtained stool and vomitus specimens, both of which contained the first larvae which were studied. During these spells it was difficult to obtain relief with fairly large doses of opiates. Following this

observation she was given santonin by mouth and colonic irrigations containing thymol. Many larvae were recovered after this, all of which were dead. Following the attacks of diarrhea the patient had a number of severe hemorrhages. Tetrachlorethylene capsules were given by mouth but they caused gastric distress. In the hospital a duodenal tube was passed and tetrachlorethylene was injected beyond the stomach. For a few weeks there was apparent improvement, but the same attacks recurred, with the passage of larvae by vomiting and bowel discharge. In addition to the severe hemorrhages from the bowel, the patient vomited blood. There were bleeding hemorrhoids. It was necessary to give two blood transfusions in September, 1931, and again after another hemorrhage in November, 1931.

Once during the summer after tetrachlorethylene was given through a duodenal tube, 1,000 c.c. of a solution containing Epsom salts was administered at a temperature of 110°F. This gave no permanent result. At Christmas time, 1931, the patient found it necessary to go to the southern part of the state where her condition has remained unchanged.

The Larvae

Specimens of fly larvae as stated above were brought to the Medical Entomology Laboratory of the University of California on March 31, 1931. Two full grown larvae placed in a receptacle with dry sand, pupated, one during the following night, and the other April 1. The first winged fly emerged April 10, and the second, April 11. These were both blue bottle flies, *Calliphora* sp.

The second lot of larvae was received May 12. These were contained in very liquid feces and were less than half grown. Fifteen of these larvae were carefully transferred to a small piece of fresh fish in a jar with dry sand and the cover of the jar sealed with vaseline. The larvae grew rapidly and pupated May 22. Seven adult flies emerged on June 4 and 5: these were green bottle flies, *Lucilia* sp. Three days later seven other flies emerged which belonged to still another genus, namely *Sarcophaga,* a species of larviparous grey flesh fly. The carefully sealed jar fully excluded any possibility of contamination on the part of flies from the outside, and the facts of the life history of these two species pointed positively to their origin as already explained.

On July 28, 1931, another lot of larvae was brought to our laboratories. These were in a specimen of stool, also very liquid. Three fully grown larvae were transferred to a jar with dry sand as before and on July 30 one pupated, the others died, and on August 11 an adult fly emerged which proved to be another blue bottle, *Calliphora* sp., like those of the first lot received, except that this specimen was decidedly undersized.

Discussion

The food habits of the three genera of flies involved in this case of intestinal myiasis would seem to indicate that the original infection was due to the ingestion of cold meat, possibly pork in some form. The genus *Sarchophaga* is a strongly carnivorous group of flies which supports this theory, although the two other genera, *Lucilia* and *Calliphora,* are more omnivorous. The recurrence of violent symptoms with egestion of larvae in vomit and stools would ordinarily point to repeated infections like the original infection, but the fact remains that the patient lived in a way that would seem to preclude repeated infestations.

The other alternative explanation of the long period of maggot infestation and the periodic recurrence of violent symptoms is that of pedogenesis, *i.e.*, the production of other larvae on the part of fully grown larvae already in the digestive tract. Normal reproduction following the usual sequence of events, pupation, emergence of adult flies, fertilization, and egg laying (or viviparous larval production) all within the intestine of a human being, is extremely difficult to believe. Certainly there were broods of very young larvae at intervals, at which time also full grown larvae were present. No examination was made of these mature larvae for evidences of pedogenesis.

At least one instance of pedogenetic reproduction has been reported for *Calliphora*, that by Parker[3] (1922), who states, "The increases .... led me to believe that *Calliphora erythrocephala* occasionally multiplies in an unusual way, and that this way is not polyembryony but pedogenesis".

In retrospect the patient must have had the condition of myiasis for a number of years because of the similarity of the many attacks. The condition complicated the protozoan infestation. There are at least three outstanding facts: (1) The condition was demonstrably present for at least a year, historically present for many years. (2) The attacks came at quite regular intervals, associated with great abdominal distress, with the passage of larvae by mouth and bowel. Following these spells there would be a period of comparative quiescence to be followed by the same sequence with the hemorrhages. (3) During the past year the patient lived in a clean modern home where the food was handled in a sanitary manner, and during the many times we were in the home no flies were seen. In view of these facts it seems impossible to explain the situation except on a basis of constant reproduction of the larvae within the gastro-intestinal tract, reaching a stage of maturity at intervals when the attacks would occur.*

Unfortunately the several species of flies involved in this case have a rather wide distribution, otherwise if one or more of these species were localized particularly in relation to Texas where the patient lived prior to coming to California, evidence would be at hand confirming our belief that this was a case of intestinal myiasis of long standing,—a very remarkable instance.

Our effort is now being directed toward a study of pedogenesis in the flesh flies. If we can produce artificial conditions simulating the digestive tract and can induce pedogenesis then, at least, a forward step has been made in the solution of our problem, but there would still remain to be had a

*Note by the Editor: In response to inquiry as to the completeness with which extra-corporal contamination had been excluded, Dr. Gilbert replied as follows:

"The specimens of feces sent to Dr. Herms were obtained either here at my office or while the patient was in Peralta Hospital. There was absolutely no chance of error in obtaining the specimens. They were obtained from defecation, from vomitus and from the rectum through a proctoscope. The anamnesis is long and the specimens were obtained more than a dozen times under the above conditions, usually associated with severe clinical attacks of diarrhea and vomiting."

reason for the incomplete response to treatment, made difficult because of severe complications.

Withal, the possibility of repeated ingestion of larva- or egg-infested food, though hard to believe under the circumstances, is still not completely ruled out.

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Familial Congenital Clubbing of Fingers and Toes

Report of a Case

By Oscar B. Ragins, M.D., and E. B. Freilich, M.D., *Chicago, Illinois*

CONGENITAL familial clubbing of fingers and toes is apparently a rare condition. A review of literature revealed no report of such conditions. We therefore thought the present example worthwhile reporting.

Mr. B., 34 years old, presented himself for examination with minor complaints of gastro-intestinal origin. During the course of examination, the peculiar clubbing of his fingers and toes was noted. There were no abnormal findings in his heart or lungs. Except for a slight tic of the palpebral muscles of his left eye, the physical examination was essentially negative.

The patient related that his sister, father, and paternal uncle have identical clubbing of their fingers and toes. He had no information as to the presence of this condition in any of his grandparents.

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From the Out Patient Department, Mount Sinai Hospital, Chicago.

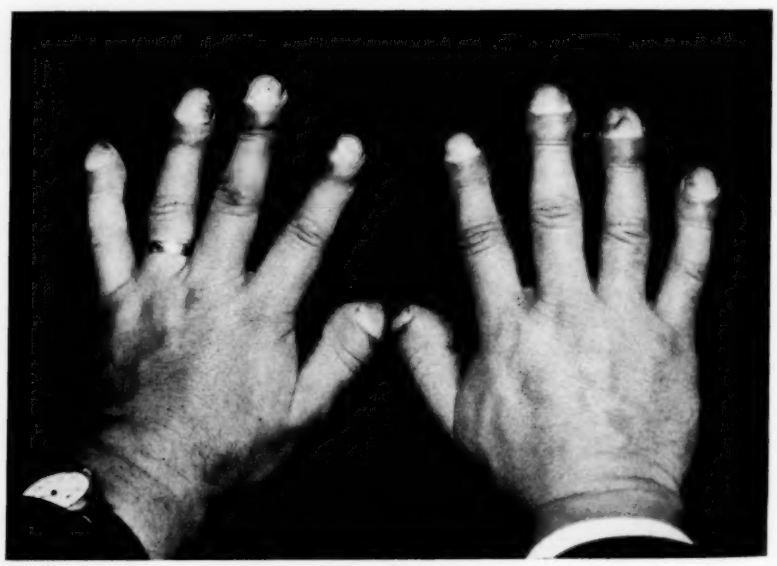

Fig. 1 Congenital clubbing of the fingers in a male patient, whose father, paternal uncle, and sister presented an exactly similar condition.

X-ray study of various parts of his skeleton and cranium revealed that the distal phalanges of the upper and lower extremities show slight enlargement, but proportionate to the other bony structures. The middle phalanx of the toes is short and broad. There is thickening of the cortex and the periosteum of the radius, thickening and proliferation of the periosteum and cortex in several regions of the tibiae and fibulae, and small exostoses in several regions of these bones.

It was noted by comparing the photographic picture and the x-ray of the hand that the clubbing of the fingers is much out of proportion to the deviation from the normal structure of the distal phalanges. Therefore the clubbing in this case affects mainly the soft tissues.

Complete Situs Transversus With Auricular Fibrillation and Flutter

Report of a Case

By Harold A. Robinson, M.D., *Detroit, Michigan*

THIS case is reported because of its interesting electro-cardiographic findings. A thorough search of the literature reveals no previous similar case reported. There are many cases reported in the literature of complete situs transversus with electrocardiographic depictions of dextrocardia. Some of them are associated with pathologic conditions of the heart, for the most part, congenital anomalies. Other case reports are of situs transversus associated with diseases other than those of the heart.

A discussion of complete situs transversus and auricular fibrillation and flutter will not be taken up here, having been thoroughly discussed in other reports in the literature.

In the absence of other congenital anomalies, there is no reason to expect an individual with complete situs transversus to differ from the normal individual in relation to health and disease. Postmortem examinations, operative reports, study of patients with complete situs transversus afflicted with systemic disease or in health, show them to react in the same manner as the normal individual. So that in complete situs transversus with auricular fibrillation and flutter, we would not expect that individual to differ from a normally developed individual with auricular fibrillation and flutter. And such is the case.

However, we would expect the electrocardiographic depictions to differ. In dextrocardia the electrocardiographic findings are inversion of P, QRS, and T waves in lead one. When associated with auricular fibrillation and flutter we would expect an inversion in lead one of the fibrillation and flutter; and such is the case. But an examination of the electrocardiogram without the history of dextrocardia would lead us to make another diagnosis as will be shown later.

Case Report

S. B., a female, white and of Roumanian birth, 40 years of age, and married, was first seen April 26, 1931. Her complaints were pain in heart, shortness of breath, and palpitation of heart.

Past history: The patient denied having had rheumatic fever, chorea, influenza, scarlet fever, diphtheria, pneumonia and pleurisy. She had had occasional head colds and sore throat in winter. An abdominal operation, or pelvic, was done in 1918, but she does not know what was done. She was not told of visceral inversion.

Catamenia: Onset of the menses was at 13 years of age; the periods were regular.

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every 28 days, of 3 to 5 days duration. Menses have been irregular since the onset of the present illness.

Family history: Her father and mother are dead, of causes unknown to the patient. She knows nothing of constitutional diseases in the family.

Marital history: Her husband is living and well. They have been married 14 years. One child died at the age of 4 months. The cause of death is unknown to the patient. There were no other pregnancies.

Occupation: Housework.

Present illness: The patient states that previous to January 1, 1931, she felt perfectly well. At that time she suffered a bad cold and had an abscessed tooth extracted. Since then she has noticed progressively increasing dyspnea, palpitation, and edema of the lower extremities; also associated weakness and dizziness when ambulatory. For two weeks before the time when she was first seen, she noticed a "flopping around" of the heart at times, and experienced occasional sharp pain over the normal cardiac area, to the left of the sternum radiating to the region of the left scapula.

Physical examination, April 26, 1931. The patient was seen lying in bed, obese, flushed, dyspneic in bed, not appearing acutely ill, with mitral-type facies, not cyanotic and of cheerful disposition. Her eyes reacted to light and in accommodation. There was a slight injection of the pharynx; the tonsils were present but did not appear diseased.

Lungs: Resonance was impaired and breath sounds absent in the lower right chest anteriorly. Normal resonance and breath sounds were found in the cardiac area. Posteriorly the lung fields were clear throughout. There were no râles.

Heart: The left border of dulness was located one fingerbreadth to the left of the sternal margin. The right border of dulness was in the right axillary line. The apex impulse was felt in the right fifth intercostal space, almost out to the axillary line. The heart sounds were very distant in the usual cardiac area but were heard very distinctly, also, in their corresponding positions on the right side. The rhythm had a definite irregular irregularity. No definite murmurs were heard. A_2 was greater than P_2. There was no increase in the retromanubrial dulness.

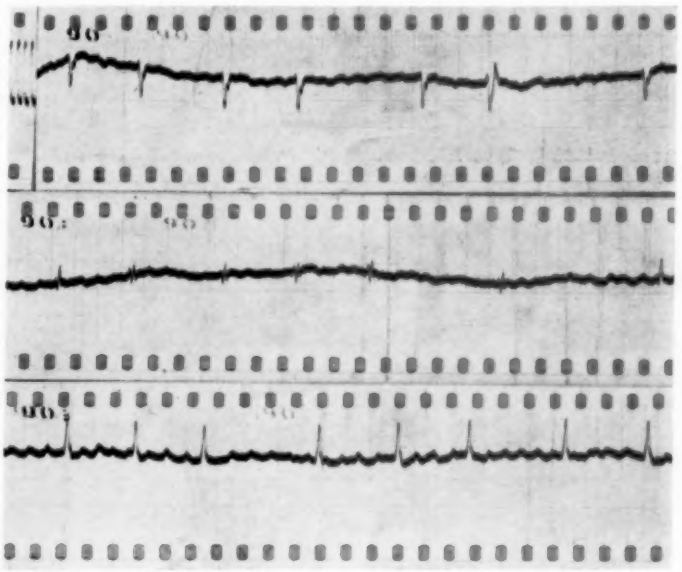

FIG. 1. Electrocardiogram, April 26, 1931. Rate 110. Auricular fibrillation and flutter, Dextrocardia. Myocardial damage. Extra systoles. Inversion P, QRS and T waves in lead I. Slurring and notching of QRS complex.

The blood pressure was 120/60 in both arms.

Abdomen: There was a lower right paramedian scar, but no masses, tenderness, or rigidity. The liver dulness was on the left side. The spleen and kidneys were not palpable.

Extremities: Pitting edema was present in both ankles and feet.

Laboratory data: Blood: hemoglobin, 86%; red blood cells, 4,550,000; white blood cells, 7,600; 81% polymorphonuclears; 17% lymphocytes; 2% monocytes. Urine: yellow color; acid reaction; specific gravity, 1,015; negative for sugar; negative for acetone.

Progress notes: April 29, 1931. Patient has had 26 c.c. of tincture of digitalis since entering the hospital. She has headaches and feels nauseated. Coupled beats are present.

May 1, 1931. Ringing ears and headache from quinidine. (See table for medication.)

May 4, 1931. Heart slow and fibrillating, but well compensated. The patient wished to go home, and was discharged with tincture digitalis, twenty minims three times daily. No symptoms of overdigitalization were present.

X-ray reports: (Dr. Reynolds): April 28, 1931. Definite dextrocardia with slight enlargement of the cardiac shadow, heart occupying a transverse position. The lung fields are clear.

April 30, 1931. Fluoroscopic study of the chest shows a definite dextrocardia, the apex of the heart being almost in contact with the thoracic wall, indicating definite enlargement of the cardiac shadow. A small quantity of opaque meal was administered, which shows the stomach on the right side and the liver on the left. This is conclusive evidence of a situs transversus.

The patient was seen at intervals after discharge from the hospital, but not as often as advised because of poor coöperation. As soon as she felt comfortable she neglected treatment. She was advised rest in bed, light diet, and tincture of digitalis, fifteen minims three times a day. On September 21, 1931 she stated that she had taken

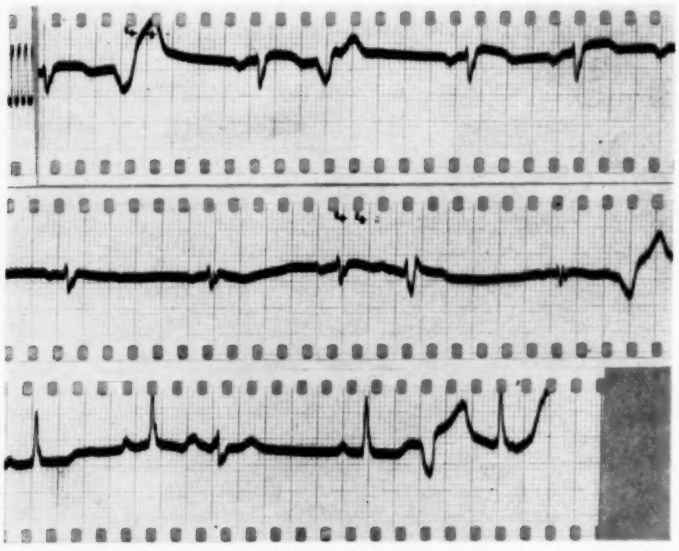

FIG. 2. Electrocardiogram, July 18, 1931. Rate 70. PR-0.16 second. QRS-0.10 second. RT-0.28 second. Inversion of P, QRS and T waves in lead I. Auricular fibrillation and flutter. Dextrocardia. Severe myocardial damage. Extra systoles. Slurring and notching of QRS. Positive ST in lead I. Negative ST in lead III. Frequent extra systoles may be due to over digitalization.

DIGITALIS AND QUINIDINE

DATE	MEDICATION	AMOUNT	TIME	PULSE RATE	NOTES
April 27, 1931	Tr. Digitalis	drams 2	10 a.m.	60	
	Tr. Digitalis	drams 1	2 p.m.	68	
	Tr. Digitalis	drams 1	6 p.m.	60	
April 28, 1931	Tr. Digitalis	drams ½	8 a.m.	56	
	Tr. Digitalis	drams ½	12 noon	60	
	Tr. Digitalis	drams ½	4 p.m.	58	
	Tr. Digitalis	drams ½	8 p.m.	58	
	Tr. Digitalis	drams ½	8 a.m.	88	Nausea and headache
May 1, 1931	Quinidine	grs. 6	9 a.m.	48	
	Quinidine	grs. 6	12 noon	50	
	Quinidine	grs. 6	4 p.m.	46	Ringing ears
May 2, 1931	Quinidine	grs. 6	9 a.m.	52	Ringing ears, headache
	Quinidine	grs. 6	1 p.m.	48	
May 3, 1931	Tr. Digitalis	mm. 20	6 p.m.	52	
	Tr. Digitalis	mm. 20	8 a.m.	46	
	Tr. Digitalis	mm. 20	12 noon	42	
	Tr. Digitalis	mm. 20	4 p.m.	42	

no medication for two weeks, and complained of return of symptoms as before. She was advised to remain in bed and continue digitalis. She was seen at intervals thereafter. While she was well compensated and went about with comfort, the auricular fibrillation and flutter were still present. In November, 1931, she decided to return to Roumania against advice. Soon after arrival there she was placed in a hospital and expired January 20, 1932.

The electrocardiographic depiction is a combination of auricular fibrillation and flutter, severe myocardial change and dextrocardia. The evidence for complete situs transversus comes from physical examination and is verified by x-ray findings which are conclusive. The electrocardiographic curves could be readily explained by mitral stenosis with right ventricular preponderance and auricular fibrillation or impure flutter. For this reason the findings are very interesting, for no other instance of this particular combination is known to the author.

SUMMARY

1. This case is reported because of the very interesting combination of dextrocardia with auricular fibrillation and flutter.

2. With this combination a diagnosis based upon electrocardiographic evidence alone would be mitral stenosis with right ventricular preponderance and auricular fibrillation or impure flutter.

3. There is no case report in the literature of this particular combination.

A Medical Poet of the Middle Border, William Savage Pitts, M.D.

By Louis H. Roddis, *Lieutenant Commander, Medical Corps, United States Navy*

THERE are numerous English and American poets whose works are voluminous and who like Shakespeare, Milton, Byron and Longfellow are as notable for the quantity as for the quality of their verse. On the other hand there are not a few who owe their fame to almost a single song. Such are Gray with the "Elegy Written in a Country Churchyard", Cooke whose "Florence Vane" has been translated into more modern languages than there are verses in the poem, Lady Scott's "Annie Laurie", Foster's "Swanee River", and Payne's "Home, Sweet Home". In these latter the wedding of words and music has given the verses a double charm and to this fact at least some of their popularity is due.

Dr. Pitts was one of these poet composers whose fame rests upon a single poem united with an air not soon forgotten. His song, "The Church in the Wildwood", has immortalized a little weathered frame church in a tiny Iowa village, has made it the rival of the Little Church Around The Corner in respect to the number of weddings held there, and leads nearly a hundred thousand people to visit the locality annually. Something about the country doctor who wrote the poem and the circumstance under which it was produced may be of interest.

William Savage Pitts was born at Lums Corners, Orleans County, New York, August 18, 1830. His parents came to Wisconsin when he was a boy. His medical training was obtained at Rush Medical College in Chicago where he received his degree in medicine in 1868. After 1862 he had made his home in Fredericksburg, Iowa, and he returned there to begin the practice of medicine. In a short time his buggy was a familiar sight on the roads of Chickasaw County around Fredericksburg, Nashua, New Hampton, and Bradford. One of his old buggies is still in use on a farm near Fredericksburg. He was a great lover of horses and always had several fine animals. One of his favorites was a bay mare with white markings named "Babe". He drove her for sixteen years through daylight and dark, snowdrifts and rainstorms. He expressed his regard for her once by saying "That

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Note by Editor: This is the fourth in a series of sketches of medical poets by the author. The subjects of those preceding were Joseph Rodman Drake, Oliver Wendell Holmes, and Oliver Goldsmith.

mare is just like one of the family". She was then twenty-one years old.

Dr. Pitts was a typical country doctor of the old school, the friend and counselor of the community as well as a physician, known to the whole countryside, their help in times of accident and sickness, birth and death. The country doctor in farming communities of the middle west in those early days saw many hardships. Called at all hours and in all weathers, to make long drives over the worst of roads, to meet all sorts of medical, surgical and obstetric emergencies with poor facilities and untrained assistants, without professional consultation and encouragement, the old country doctors had to be men with physical, mental, and moral stamina, to meet their tasks and accomplish them with credit. That they usually were such men and that they did perform well the difficult duties of their calling is well known to millions who were their patients. With our refined methods of diagnosis, our laboratories and x-rays, we are apt to disparage their diagnostic methods, but necessity sharpened their powers of observation to such an extent that in the field of physical diagnosis, particularly in inspection and palpation, they were probably vastly superior to our present generation of medical men. Some of their homely therapeutics are also not to be despised. Bread and milk, and flaxseed poultices were not bad dressings for the preincisional stage of cellulitis and the rubbing of the chest with camphorated oil and swathing in flannel gave comfort and encouragement, at least, in acute pulmonary conditions. We often overlook the fact in our more scientific methods that comfort and encouragement are valuable healing agents. Liberal inunctions of goose grease made babies of the last century fat and healthy even though nothing was known of fat soluble vitamins. As a matter of fact goose grease inunctions and cod liver oil, both commonly used by the country doctors of the older generation, were going completely out of style until the discovery of vitamins brought them into use again. A hot footbath with a little mustard or a little bran in the water, a hot lemonade with a little whiskey in it, five grains of quinine or Dover's powder, and a nice warm bed are still as good treatment for a severe cold at its onset as any that we ourselves with all our laboratory training have to offer.

If the country doctor had many hardships there were many compensations as well. The position of helper in times of distress and suffering, and of holder of that vast body of confidential information that even the religious confessional does not receive gave him a unique place. He was one of the leading men in the community, probably the most respected and looked up to person in it. He always had the best that the place afforded. His compensation in money might not be munificent but it was ample, and where money was not available and he was paid in kind, the choicest garden truck, potatoes, wood, butter, cheese, bacon, ham, quarters of beef, halves of hogs, poultry, head cheese, country sausage, buckwheat honey, and other similar commodities went to his door. His home was usually the best in town. This was true of Dr. Pitts. His large white house is still standing in Fred-

ericksburg. The rooms are spacious and during the forty years that he lived there were full of old fashioned furniture. In the gable at the front was the word "Home" in large gilt letters. The house stood in a big plot

FIG. 1. Doctor W. S. Pitts, June, 1916.

of ground with numerous large shade trees around it, and in the rear there was a barn with a small pasture for his horses. His office was in two of the rooms of his residence.

Dr. Pitts was first married in December, 1859, to Ann Eliza Warren and it is to her that reference is made in the last two verses of the song. Many of the older residents of Fredericksburg remembered her well. She was a very fine looking woman, of medium height, and with dark brown hair and handsome dark brown eyes. She died in 1886. Some years later he married again, this time to a widow, Mrs. Martha Grannis, who also predeceased him.

In appearance Dr. Pitts was tall, well built, strongly made and active. His eyes were blue, rather deeply set and shaded by very heavy eyebrows. He wore a full beard. He was greatly interested in music, often taught a singing school, was the leader of the local band at Fredericksburg, and the leader of the choir of the Baptist Church there for thirty-five years. He had a fine tenor voice and frequently sang solos in church, including his own famous composition. In after years, when the song was known around the world, Dr. Pitts often told how he came to write it and the manner in which it came to be identified with the real "Little Brown Church in the Vale". This is the account in his own words:

"One bright afternoon of a day in June, 1857, I first set foot in Bradford, Iowa, coming by stage from McGregor. My home was then in Wisconsin. The spot where the Little Brown Church now stands was a setting of rare beauty. There was no church there then but the spot was there waiting for it. When back in my home I wrote the song, The Little Brown Church in the Vale. I put the manuscript away. In the spring of 1862, I returned to Iowa and settled at Fredericksburg, inasmuch as my wife's people were there. In the winter of 1863-64, I taught a singing class in Bradford. We held our school in the brick building known as the Academy. In the years of 1859 and 1860, the good people of Bradford were determined

to build a church. I will not take time to tell of the trials, the disappointments and the successes that followed; suffice it to say, by the early winter of 1864, the building was ready for dedication.

"While I was holding the singing school, near its close in the spring, the class went one evening to the church. It was not then seated, but rude seats were improvised. My manuscript of the song I had brought with me from Wisconsin had never been sung before by anyone but myself. I sang it there. Soon afterwards I took the manuscript to Chicago, where it was published by H. M. Higgens. It won a speedy recognition locally and with years won its way into the hearts of the people of the world. Soon after its publication the church at Bradford which had been painted brown, (for want of money to buy better paint, some say) became known as The Little Brown Church in the Vale. My hope is that it will stand for a thousand years and call the Old Man and his descendants to worship.

"Under the circumstances, what more natural than that the little church at Bradford, Iowa, painted brown, and the song, The Little Brown Church in the Vale should be wedded and known as one and the same. Some people may try to rob the little church of its fame, but as long as it stands it will be known as The Little Brown Church in the Vale."

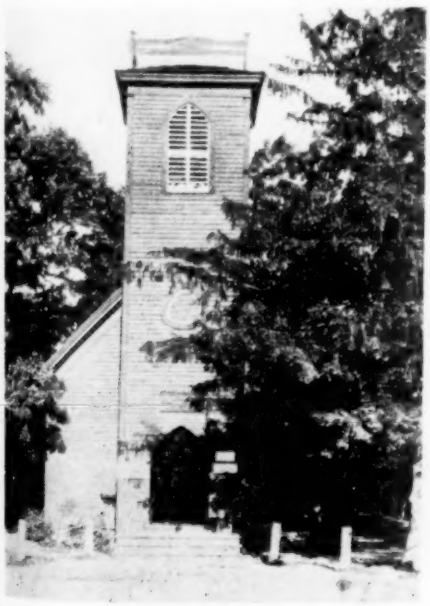

Fig. 2. The Little Brown Church near Nashua, Iowa.

This is the song as Dr. Pitts wrote it and as he first sang it in the newly erected "Church in the Wildwood".

There's a Church in the valley by the wildwood,
No lovelier place in the dale,
No spot is so dear to my childhool,
As the Little Brown Church in the vale.

O, come, come, come, come,
Come to the Church in the Wildwood,
Come to the Church in the dale,
No spot is so dear to my childhood,
As the Little Brown Church in the vale.

How sweet on a bright Sabbath morning,
To list to the clear ringing bell,
Its tones so sweetly are calling,
O, come to the Church in the vale.

There, close by the Church in the valley,
Lies one that I loved so well,
She sleeps, sweetly sleeps, 'neath the willows,
Disturb not her rest in the vale.

There close by the side of that loved one,
'Neath the tree where the wild flowers bloom,
When the farewell hymn shall be chanted,
I shall rest by her side in the tomb.

It is thus seen that the writing of the song preceded the building of the church. As Dr. Pitts states, the poem was written in 1857. The church was not begun until 1859, and not completed until 1864. Bradford, the site of the church is now deserted, but in the early 1850's it was a place of some note, was an early Indian trading point, the first county seat of Chickasaw County, and on the stage line west toward Des Moines and Council

Bluffs. There was an Academy which made it a local educational center, a brewery, a tannery, and a cabinet organ factory. The long main street was lined with stores, saloons and offices. The town was located in the valley of the Cedar River, justly celebrated as one of the most beautiful parts of Iowa. In 1859 a young Congregational minister, the Reverend J. K. Nutting, began the project of building a church on the spot near the edge of town which had attracted the attention of Dr. Pitts as a "setting of rare beauty" and which was still covered with oaks and evergreens. A "bee" was organized to quarry rock for the foundation. The breaking out of the Civil War prevented for a time the completion of the church. Finally another "bee" cut native timber furnished free by a member. The dimension lumber and sheeting were taken from fifty foot red oaks growing near the site. A local sawmill sawed the logs without charge and a volunteer force of carpenters erected the building. There was no money for the finishing lumber and the pastor wrote to a friend in the east who was a pastor of a wealthier church. This was the Reverend John Todd of Pittsfield, Massachusetts. A check for $140 from the children of the Sunday School was received and the eastern pastor also made arrangements for a loan of $300. This loan was not paid off until 1926, after the note had run for sixty-two years. The finishing lumber for the church was hauled by wagon teams from McGregor, Iowa, on the Mississippi, more than eighty miles away. The church was dedicated in December, 1864, and a large picture of Abraham Lincoln hanging on the north wall reminds us of the fact that the event occurred during the administration of the Civil War President. The church bell, "the clear ringing bell" of the poem, was cast in the famous Meneely bell foundry, at Troy, New York. It was hauled by team from Dubuque, hung in a frame on the wagon so that it rang almost continuously on its way to Bradford. It was the first church bell in Chickasaw County. Its coming was an event of no small importance to the settlers and they were very proud of this great acquisition to the community.

After its publication the song became known in wider and wider circles. Its inclusion in a Moody and Sankey hymn book spread its fame around the world. In England, Scotland and Wales, and in the British Colonies, in far away Australia and New Zealand, South Africa and the "Isles of the Sea", it began to be sung and loved. Translation into almost all modern languages followed. It is said to be especially popular in Germany and Scandinavia. Then people began to visit the original of the Brown Church. Times had changed since the church was built and the town of Bradford had practically ceased to exist. In 1867, when the Illinois Central Railroad was built down the valley of the Cedar River, it missed Bradford and passed through Nashua a few miles away. Most of the population moved to Nashua, and New Hampton became the county seat. The old brick academy is now a farm home. The Bird residence, once one of the finest houses in the town and the home of the donor of the ground on which the church

stands, is deserted and falling to pieces.

But if the town declined, the church did not, and as its fame grew, more and more people began to visit it and to come there to be married. Finally in 1900 a Society for the Preservation of the Little Brown Church was organized. A pastor was assigned from the Congregational Church of Nashua and for a number of years has held both charges. Now the church in the abandoned town has become the more important of the two, with thousands of visitors and a reputation as a matrimonial Mecca. Today each new bride married in the Church in the Wildwood has the privilege of ringing the famous old bell and that it is heard pretty frequently is shown by the fact that in 1929 six hundred and forty-three couples were married there. Three hundred and twenty-one couples were married there during the first six months of 1930. On January 16, 1926, thirteen couples pronounced their marriage vows before the altar. In front of the pulpit is a little square of green carpet. This has many times been worn out and replaced. The old Bible on the altar, however, is still unchanged. An inscription on the flyleaf shows that it was presented to the church by Mrs. Mary Vinton in 1864.

The present pastor, the Reverend William Kent, has learned the marriage ceremony by heart through frequent repetition and well deserves the title of "The marrying Parson of the Middle West". Every state in the Union and many foreign countries are represented by the long chain of brides and grooms. Iowa, Minnesota, Wisconsin, the Dakotas, Nebraska, Kansas, and Montana furnish the greater number. Naturally enough Iowa leads the list and the largest number are always from the state "where the tall corn grows." Brides of the Middle West seem to take special pleasure in placing "Little Brown Church in the Vale" on their wedding announcements.

A register book is kept for visitors. More than thirty thousand have registered in a year and it is estimated that nearly as many visit the church without registering. It is believed that as many as one hundred thousand people make a pilgrimage to the spot annually.

The old bracket lamps in the church and the pews are as when first installed. On the reed organ a hymn book is always open at the "Little Brown Church in the Vale", and the singing of this song is a feature of every service. On the wall is a framed copy of the verses. The bell still calls the congregation to worship, and lovers to the holy bonds of matrimony. On Sundays during the summer months the little church is too small to hold the crowds that gather under the oaks and pines that embower it and make it still "the Church in the Wildwood".

In 1916 there was held a special reunion at the church at which Dr. Pitts, then aged 87, and the Reverend J. K. Nutting, aged 84, were present, so that the writer of the song and the builder of the church were brought together again after a lapse of nearly sixty years. A picture of them was taken standing side by side in the doorway of the church. Each delivered a short address and Dr. Pitts sang the

song he had written fifty-nine years before.

Dr. Pitts died in a hospital in New York City, September 25, 1918.

In his later years he had made his home with a son, William Stanley Pitts in New York. His death which was due largely to the infirmities of age followed a brief acute illness. He is buried in the beautiful Rose Hill Cemetery in Fredericksburg, Iowa, where a small stone marks his grave.

The following is a list of his poems. None except the Church in the Wildwood had other than local fame and a number were never published and exist only in manuscript.

"Little Fred"

"The Church in the Wildwood" or "The Little Brown Church in the Vale"

"Sabbath Bells"

"Nellie Wildwood"

"The Old Musician and his Harp"

Some others not now known.

One cannot but ask what there is about this simple poem to enable a country doctor to immortalize and make world famous a little church in an obscure deserted town. To answer that question one has but to listen to it sung by a pleasing voice or to read it over to oneself to feel that it possesses that simple yet indescribable charm which makes certain lyrics linger in the memory and in the heart, when more pretentious poetry by greater poets is forgotten. The simple yet charming imagery of the "Valley in the Wildwood" and the appeal to the feelings common to all human nature such as the longing for immortality and the desire even in death to remain united with those loved in life are other reasons for its universal appeal. Though his fame rests on a single song we may well add William Savage Pitts to the long and distinguished roll of medical poets.

Bibliographical Note

The Reverend Wm. Kent, the present pastor of the First Congregational Church at Nashua, furnished much information in regard to the life of Dr. Pitts and a number of pamphlets about the church and the poem. A good feature article on the subject appeared in the *Minneapolis Tribune* of October 3, 1926. Lieutenant H. R. Hubbard, Supply Corps, United States Navy, who spent his boyhood in Fredericksburg and knew Dr. Pitts and his family, supplied many facts. Mrs. Ida Stiles of St. Paul, who as a girl lived in Chickasaw County remembered Dr. Pitts as their family physician. When a young woman she sang in the choir of the Little Brown Church and she has contributed information of interest. Dr. Pitts's daughter, Mrs. Alice M. Tuttle of Riverbank, California, has read the article in manuscript and made a number of comments and corrections. Two other of Dr. Pitts's children are living, Mrs. Katie B. Noble of Denver, Colorado, and William Stanley Pitts of New York City.

Editorials

PROGRAM OF THE SEVENTEENTH ANNUAL CLINICAL SESSION OF THE AMERICAN COLLEGE OF PHYSICIANS

Although the program of the Annual Clinical Session, which is to be held in Montreal, February 6 to 10, has been sent through the mails to all Fellows and Associates of the College, it is printed in the present issue for the added convenience of members and non-members alike. Those expecting to attend will find it very much to their advantage to study this program in advance. Attention is invited to the significant groupings of the subjects in the General Sessions, and particularly to the emphasis which is placed upon the intrinsic constitution as a factor in determining disease. Those registering should plot their course in advance in respect to the Special Clinics and Demonstrations, some twenty-five of which are simultaneously available each morning. The necessity for early registration of choice and the wisdom of requiring clinic tickets will be apparent to all. It is to be hoped that many will avail themselves of the opportunity to visit the Library of the Medical School of McGill University, the Osler Library, and the Medical Museums at the McGill Medical Building and the Pathological Institute.

MAURICE CHARLES PINCOFFS, EDITOR OF THE ANNALS OF INTERNAL MEDICINE

It is with mingled feelings of regret and pleasure that the present editor of the ANNALS records the fact that his official duties end with the present number. There is regret like that at parting with a very close friend, or, as a better figure, with a member of one's own body; for it is impossible to edit, single handed, such a journal as the ANNALS without its becoming in a very real sense identified with one's self. There is regret at the loss of that stimulus, based on the ever-recurring necessity of surveying a long list of original papers and of periodicals and books each month. And especially is there regret that the sequence of old and new contacts made each year with hundreds of authors and investigators, scattered over the continent is to be broken. Of the coöperation, forbearance, courtesy, and friendship of his authors, the editor is fully appreciative. With all of this, however, there is a sense of satisfaction in being able to announce that by the unanimous choice of the Regents of the American College of Physicians, Maurice C. Pincoffs, Professor of Medicine and Head of the

Department of Medicine, University of Maryland, Baltimore, Maryland, is assuming the editorship of the ANNALS. For three months there has been a gradual shifting of the editorial duties from the old office to the new so that there will be no interruption in the sequence of issues.

Doctor Pincoffs was born in Chicago in 1886, and received his elementary education in private schools in that city and in Antwerp. At the University of Chicago he earned the degree of Bachelor of Science and there he completed the first two years of the medical course, during which he was awarded the Brainard prize in Anatomy. He assisted in Anatomy for one year and took special courses in Pathology under Professor Gideon Wells. The medical degree he obtained from Johns Hopkins Medical School in 1912. Dr. Pincoffs was unusually fortunate in respect to the men with whom he was closely associated in his early years in Medicine. As interne, resident, associate, and voluntary assistant, respectively, he worked with Doctors James B. Herrick, Thomas R. Boggs, Lewellys F. Barker, and John J. Abel. From 1917 to 1919 he was in military service with the British Expeditionary Force, the American Red Cross, and the American Expeditionary Force, receiving the Distinguished Service Cross and the Croix de Guerre with palm and two stars. He served at Johns Hopkins Medical School as Instructor in Medicine from 1919 to 1922, assuming the full professorship in Medicine in the University of Maryland in 1922. He is also Physician-in-Chief of the University Hospital and of Mercy Hospital. Elected as a Fellow in 1923, Dr. Pincoffs has served the American College of Physicians as Governor, Regent and First Vice President. In addition to numerous articles in medical journals and transactions, he is the author of the section on Diseases of the Peritoneum in the Oxford System of Medicine, on Visceroptosis in Tice's System, and on Diseases Due to Chemical Agents in Musser's Internal Medicine.

Thus Doctor Pincoffs, through training and experience in clinical medicine and medical education, is peculiarly fitted for the position for which he has been chosen. The ANNALS OF INTERNAL MEDICINE and the American College of Physicians are to be congratulated upon his selection and acceptance, which forecast continued success and added prestige for the official journal. May we bespeak for him the same loyal support which has been given his predecessor!

Abstracts

The Significance of Urinary Casts in Normal Persons. By HEBER C. JAMIESON, M.B. (Canad. Med. Assoc. Jr., 1932, xxvii, 607-612.)

Exercise brings about transitory changes in the normal kidney, resulting in the excretion of albumin, casts, and red and white blood cells. All of these are in excess of normal and, as a rule, the more strenuous the exercise, the more albumin, casts, and blood cells will be found. For instance, after less vigorous sports, such as badminton and

tennis, fewer formed elements and less albumin are found than after long distance cross-country running and hockey. Even after short periods of time in the lordotic posture, the excretion of blood cells is noted. In all of these tests white blood cells were found more frequently than red blood cells, and the latter more often than casts. Any condition which tends to concentrate the urine and increase its acidity may be responsible for an increase of formed elements. The medical practitioner should be on his guard not to attribute the presence of these formed elements, in the urine of normal persons, to pathological conditions.

The Hematopoietic Response in Pernicious Anemia Following the Intramuscular Injection of Gastric Juice. By ROGER S. MORRIS, M.D.; LEON SCHIFF, M.D., GEORGE BURGER, M.D., and JAMES E. SHERMAN, M.D. (Am. Jr. Med. Sc., 1932, clxxxiv, 778-782.)

The results of previous researches have seemed to indicate that the normal stomach secretes a substance (probably the same as that which Castle has shown to be present) which, while without effect on the reticulocytes when administered orally, might cause a response if it could be administered parenterally. This assumption has been tested by the intramuscular injection of neutralized sterile gastric juice and also of a concentrate of normal human gastric juice obtained by evaporation *in vacuo*. The results prove the presence in normal gastric juice of a powerful bone marrow stimulant, producing not only a marked and very rapid reticulocyte increase after intramuscular injection but also a rapid maturation of the red cells. For this anti-anemic substance, which is probably a hormone, the name *addisin* is proposed. This active principle, lack of which in the gastric juice would seem to be the cause of pernicious anemia, is found in the supernatant fluid, but not in the precipitate, which forms in the process of concentrating gastric juice. It is thermolabile, dialyzable, and exhaustible. Acetone extracted gastric juice of swine has been found to give less marked local and general reactions than the preparations first used.

Diathermy in the Treatment of General Paralysis and in Wassermann-Fast Syphilis. By JAY FRANK SCHAMBERG, M.D., and THOMAS BUTTERWORTH, M.D. (Am. Jr. Syph., 1932, xvi, 519-534.)

Under malarial therapy for paresis, about one-third of the patients go into a good remission, one-third into a partial remission, and one-third show no improvement. The average mortality with malarial therapy is about eight per cent. The authors have treated 26 cases of refractory syphilis by means of fever produced by diathermy. Of nine paretics who completed the treatment, six, or 66 per cent, improved; three returned to their former occupation. The single case of taboparesis treated showed marked improvement as did also the one case of cerebrospinal syphilis. Of the three cases of tabes dorsalis, one was relieved of his pains entirely and improved physically; a second patient improved physically, his pains decreased, but there was no improvement in his ataxia; the third became progressively worse. The two cases of interstitial keratitis showed considerable improvement, but in both, diathermy was augmented by mercurial inunctions and bismuth intramuscularly. Seven patients with Wasserman-fast syphilis showed no change in their serologic findings after treatment, although only one to seven months had elapsed since their discharge from the hospital.

Liver Function in Hyperthyroidism. By S. S. LICHTMAN, M.D. (Arch. Int. Med., 1932, l, 720-729.)

Clinical evidence of disturbance of the liver in hyperthyroidism is afforded by occasional cases of icterus in association with thyrotoxicosis for which no other cause can be discovered. Hepatic changes, even a fully developed interlobular cirrhosis, have been discovered in some cases of hyperthyroidism. Thyroid substance, or thyroxin, causes the glycogen to disappear from the liver. The author investigated the liver function in a series of twenty consecutive cases of hyperthyroidism, making use, among other methods, of an original cinchophen oxidation test. A disturbance in the oxidation of cinchophen was demonstrated in 16 of the 20 cases, the

results indicating moderate rather than severe impairment of the capacity of the liver to oxidize this substance. No apparent relationship between the degree of functional impairment of the liver and the basal metabolic rate, the known duration of the disease, or the percentage of weight lost was found. In individual cases, however, there appeared to be a tendency for the function of the liver cells to improve as the basal metabolic rate returned to normal. The galactose tolerance test gave no indication of a disturbance of hepatic function. There was little evidence of appreciable disturbance of the excretory functions of the liver as determined by studies on the icterus index, bilirubinemia, urobilinuria, and urobilinogenuria.

Effect of Dietary Calcium and Phosphorus on Toxicity of Lead in the Rat: Rationale of Phosphate Therapy. By DAVID H. SHELLING, (Proc. Soc. Exp. Biol. and Med., 1932, xxx, 248-254.)

The rationale of the use of calcium compounds in the treatment of lead poisoning depended upon the following facts: First, the solubility of lead phosphate was found to be analogous to that of calcium phosphate; hence it was believed that lead might be deposited in bones in the same manner that lime salts are. Second, it was believed that the deposition of lead in the bones could be increased by furthering the process of calcification through the administration of calcium. Third, the prompt relief of lead colic through the intravenous administration of calcium chloride was thought to add additional evidence that calcium "drives" lead into the bones. It is now thought that this effect is produced by relaxation of the intestinal musclature. Various studies upon the effect of lack of balance between calcium and phosphorus in the dietary make it seem obvious that the addition of calcium to lead diets which contain an inadequate amount of phosphorus does not lead to improved deposition of either calcium or lead phosphate in the bones, but, on the contrary inhibits such a process. If the aim of therapy in lead poisoning is to deposit lead, or to excrete it in an insoluble, and hence innocuous, form, an abundance of phosphorus or of foods containing phosphorus should be supplied. The correctness of this assumption was tested experimentally in rats. Eight groups of animals were fed 1.5 gm. per cent of $2PbCO_3.Pb(OH)_2$ with and without the addition of either $CaCO_3$, Na_2HPO_4, or $MgCO_3.Mg(OH)_2$. Four of the groups received the respective diets with, and four without, the addition of viosterol. In the group not receiving vitamin D, weight and longevity were most adversely affected in the sub-group receiving lead and magnesium compounds, with decreasing effects, in order, in those receiving calcium and lead compound, lead compound alone, and lead and phosphate. In fact, those receiving Na_2HPO_4 with lead gained weight steadily and appeared normal. With the exception of those in the Na_2HPO_4 group, which lived and did well, all of the animals receiving vitamin D died sooner than the corresponding controls not receiving the vitamin. It may be that vitamin D diverted calcium phosphate into the bones and allowed lead, not combined with phosphate, to circulate freely; whereas in the Na_2HPO_4 group the phosphate was adequate for deposition and excretion of both calcium and lead as phosphates. It would seem, therefore, that phosphorus is essential for the deposition of lead and that subsequent deleading can best be accomplished by a diet low in calcium and relatively high in phosphorus.

Reviews

Internal Medicine, Its Theory and Practice. Edited by JOHN H. MUSSER, B.S., M.D., F.A.C.P. 1316 pages, illustrated. Lea & Febiger, Washington Square, Philadelphia, 1932. Price, $10.00, net.

The appearance of a new single-volume text book of medicine is always an event of importance in the field of medical publication. The text book of medicine is the corner stone in the building of a medical student's clinical library. It is probably more frequently referred to by the general practitioner than any other book. The consultant will read it to see what progress he may have overlooked in subjects that are not included in his special interests. There is no medical book which, if successful, will be more widely read than such a text book and none which may exert a greater influence in its generation on the level of medical practice.

The text books of recent years tend to be national in character rather than personal. Osler's text book was Osler and the experience of Osler's clinic. Cecil's text book is a summary of American medicine as Prie's is of British medicine. In this new volume Musser has brought together what might be called the medicine of American Medical Schools. The authors, including the editor, are all active teachers of medicine of professorial rank in the leading medical schools of the country. The restriction of the number of contributors to twenty-seven has allowed each one to cover completely a relatively large and relatively autonomous section of internal medicine. The reviewer feels that these sections have thereby gained something of a personal quality and a certain sense of perspective not otherwise attainable. This is, of course, particularly true of such sections as those on mental diseases and on gastro-intestinal diseases in both of which a perspective and an individual point of view are especially desirable. Most of the authors have introduced their subject by a general discussion in which they have summarized the common features of the group of diseases to be described — their etiological factors, their pathologic physiology and, in some instances, their relative social importance. These introductions add greatly to the value of the volume. Many are models of concise clear statement of essential known facts. In future editions similar introductions might well be added to those chapters in which they are lacking.

The book is divided into four parts. Part I deals with the infectious diseases. The diseases of bacillary, coccal, virus, rickettsial, spirochetal, protozoal, metazoal and unknown etiology are dealt with in separate chapters. This is a logical arrangement. It also seems wise to have made an exception to this order in grouping in one chapter the contagious diseases of childhood. It is less easily understood why the subject of tuberculosis should be omitted from this part of the book and dealt with only under the heading of pulmonary tuberculosis. There are few criticisms to be made of these excellent chapters on the infectious diseases. The treatment of the important subject of lobar pneumonia seems too summary. In discussing the pneumococcus types only the first three and group IV are mentioned. No statement is made of possible harmful effects from digitalis. The use of concentrated sera is dismissed with the statement that Cole has said that whole horse serum is superior.

Part II covers the systemic diseases. The chapter on diseases of the heart and pericardium is clear, well proportioned, and conservative. The etiological types of heart disease are well presented; and the various valve lesions and arrhythmias are separately discussed. An equal level of excellence is maintained in most of the other chapters.

The presentation of the diseases of the endocrine glands is especially concise and informative. In the otherwise admirable chapter on the respiratory diseases the brief and inadequate account of empyema seems regrettable. Certain of the blood diseases also receive scant consideration. A surprising clinical picture of agranulocytosis is presented; certainly not that most commonly seen.

Part III is devoted to diseases of nutrition, allergy, metabolism, physical and chemical agents. These chapters are clear summaries of the more important aspects of the disease processes concerned. It is perhaps unavoidable that most of the space is given to description of the chemical, physical, metabolic and immunological backgrounds, and that the clinical descriptions are correspondingly brief.

Part IV is on diseases of the nervous system. These are dealt with in two chapters. The first on mental disorders covers this field somewhat more thoroughly than is usual in text books of medicine. The psychoses are divided into those associated with organic disease, those of toxic origin, and the functional psychoses. The limited space devoted to the chapter on the organic diseases of the nervous system has resulted in a very brief discussion of many of them. The pages given to anatomy and methods of examination could be utilized to better advantage in amplifying the clinical descriptions. It is customary to include a brief discussion of anatomy and methods of examination in a chapter on neurological disease, but in reality it is no more appropriate than it would be to insert a general discussion of physical diagnosis or of clinical pathology in the other sections of the book. The inclusion of a discussion of head injuries and the emphasis given subarachnoid hemorrhage seem excellent features.

Minor criticisms which may be offered do not affect the estimate of the book as a whole. It is a valuable presentation of the present status of our knowledge of internal medicine. It is unusually readable and stimulating. The reviewer feels that it can be highly recommended to students, to teachers, and to practitioners of medicine.

M. C. P.

Accidents, Neuroses and Compensation. By James H. Huddleson, M.D., Associate in Neurology, Columbia University, and Attending Neurologist, Neurological Institute, New York, with a Forword by J. Ramsay Hunt, M.D., Sc.D., Professor of Neurology, Columbia University. ix + 256 pages. Williams and Wilkins Co. Baltimore, 1932. $4.00.

The passing of each year is accompanied by a startling increase in the legal and medical perplexities revolving about essentially psychogenic disorders resulting from or associated with physical injuries. With the steady growth of various and conflicting types of industrial compensation laws, these problems have established themselves among the most difficult ones with which the medical profession must contend. They represent a boundary zone in which honesty and knavery are most intimately mingled and keen indeed must be the physician's analysis if he is to insure justice for patient and employer. The author approaches his problem fortified by a broad background of experience replete with illustrative material. From his contact with that richest of all sources of traumatic neuroses, the World War, he is able to contribute substantially to the understanding and rationalization of many forms of neurosis. The book follows the usual form of special disease presentation; etiology, symptomatology and diagnosis, pathology, therapeusis and prophylaxis are discussed in a systematic manner. The treatment of the subject is in some respects encyclopedic, the various theories and conceptions concerning each important point being presented in a condensed manner with complete references to the literature. Thus the purely didactic mode is amplified so that the result is a practical source book in this particular field. To the casual reader, this method undoubtedly seems somewhat labored and to compensate there is appended to each chapter a summary giving the most important conclusions of that division. Such a procedure is rather uncommon but its effectiveness cannot be disputed. A rapid reading of these summaries will give the reader an excellent orientation so that the detailed

development may be the more clearly and completely apprehended.

Throughout the work, the legal aspects of this medical problem are emphasized and especial stress is given the relationship between the duration and character of compensation and the severity of the disease. The direct relationship between the duration of the neurosis and the time span and expectancy of compensation forms a medico-legal association which would well justify the presentation of this volume to every judge, lawyer or commission dealing extensively with workmen's compensation and industrial insurance. Forty pages are devoted to bibliography, which with the index, constitutes nearly one-sixth of the book. This high proportion is almost necessitated by the nature of the material presented, for without these divisions, in their complete form, much of its usefulness as a reference work would be lost.

J. C. B.

Treatment of Syphilis. By JAY F. SCHAMBERG, A.B., M.D., Professor of Dermatology and Syphilology in the Graduate School of Medicine of the University of Pennsylvania; former President of the American Dermatological Association; etc.: and CARROLL S. WRIGHT, B.Sc., M.D., Professor of Dermatology and Syphilology in the Temple University School of Medicine; Associate Professor of Dermatology and Syphilology in the Graduate School of Medicine of the University of Pennsylvania; former President of the Philadelphia Dermatological Society; etc. xxiv + 658 pages, 62 illustrations. D. Appleton and Company, New York and London, 1932. Price, $8.00.

To those who appreciate the complexity of the problems arising in the management of syphilis and at the same time are aware of the incidence of this disease, a book of generous size on the *treatment* of syphilis need occasion no surprise. It is believed with good reason that the 200,000 cases of syphilis which are reported annually to Public Health authorities in this country represent not more than one-fifth or one-fourth of those actually under medical care each year. In addition there are the other tens, and probably hundreds, of thousands who remain undiagnosed, or if diagnosed, are not receiving treatment. There is no practitioner nor specialist into the field of whose endeavors syphilis does not obtrude. The authors of this book believe that 15 to 20 per cent of chronic invalids in the wards of general hospitals are there because of the chronic effects of syphilis upon the internal organs. A comprehensive survey of present knowledge and experience in the management of this disease is to be welcomed. While the authoritative position of the authors in their special field would entitle them to *ex cathedra* utterance, they have given full recognition to the opinions of others. Thus an analytical survey of the entire field is presented. The clinical illustrations are well chosen but not always as well reproduced as they deserve. Little need be added as to scope of the contents of this book. It is in every respect adequate. Full discussion of "cured" syphilis and of the ever-recurring question of syphilis and marriage is provided. It is a pleasure to recommend this thoroughly scholarly book to all interested.

A Descriptive Atlas of Radiographs: An Aid to Modern Clinical Methods. By A. B. BERTWISTLE, M.D., Ch.B., F.R.C.S. Ed. Second edition, revised and enlarged. xxviii + 552 pages, 767 illustrations. C. V. Mosby Company, St. Louis, 1932. Price, $13.50.

There are many text-books and monographs for those who are specializing in Radiology, but few which are sufficiently fundamental and yet broad enough in scope to serve the needs of those who are engaged in general or special practice but who are not themselves radiologists. For such the need of sufficient knowledge to be able to understand the interpretations of others and, on occasion, to form worthwhile judgments of their own, is obvious. An extended chronology of the outstanding achievements in radio-diagnosis serves as an historical introduction. The illustrative plates, with short clinical and descriptive notes make up almost the entire volume. Plates of normal structures are placed on left hand pages and those of pathological

conditions on right hand pages only. Thus confusion is avoided and comparison facilitated. The first 57 figures are of normal skeletal structures, and include an exposition of silhouette radiographs, combining the advantages of demarcation of the soft parts with adequate detail in the bone. Congenital abnormalties are represented by 15 figures; fractures, by 99; inflammatory disease of bone, by 79; neoplasms of bone, by 27; injuries and diseases of joints, by 61; the nasal and dental regions with related structures, by 45; the alimentary system, by 171; the urinary system, by 51; the respiratory system, by 72; the nervous system, by 50; the vascular system, by 12; the thyroid system, by 8; the female generative system, by 8, and the muscles, by 11. Much of interest and value to the medical man who is not a "radiologist" can be found in this book.

Fungous-Diseases: A Clinico-Mycological Text. By HARRY P. JACOBSON, M.D., Attending Dermatologist and Member of the Malignancy Board, Los Angeles County General Hospital. With Introductions by JAY FRANK SCHAMBERG, M.D., Professor of Dermatology and Syphilology, Graduate School of Medicine, University of Pennsylvania; and HOWARD MORROW, M.D., Clinical Professor of Dermatology, University of California Medical School. xiv + 317 pages, 153 illustrations. Charles C. Thomas, Springfield, Illinois, and Baltimore, Maryland. 1932. Price, $5.50, postpaid.

Clinical mycology is presented by Jacobson with emphasis on the clinical aspect. Thus the major divisions of his book are based upon the character of the disease process, rather than upon a botanical classification. Division A is for the "primary cutaneous mycoses with (usually) no definite systemic involvement". This includes the ringworms and related condition. Division B includes the "primary cutaneous and or mucous membrane infections with frequent systemic involvement". Under this heading are found moniliasis, maduromycosis, sporotrichosis, blastomycosis, actinomycosis, and coccidioidal granuloma. The third division, C, for torulosis and aspergillosis, is characterized as "primary systemic infections with occasional instances of skin or mucous membrane involvement". The author writes from an extensive and rich experience. The subjects treated do not include all of the mycotic diseases of man of this country; but, as is evident from the foregoing lists, all of the important ones and some of the less common are presented. The clinical and bacteriological illustrations are good, those of histopathologic features are not particularly informative. This is sure to prove an extremely useful book to both practitioners and laboratory workers, for it brings together a large material much of which was hitherto available only in original sources.

A Guide to Human Parasitology for Medical Practitioners. By D. B. BLACKLOCK, M.D. (Edin.), D.P.H. (London), D.T.M. Liverpool), Professor of Parasitology, Liverpool School of Tropical Medicine, the University of Liverpool; formerly Director of the Sir Alfred Lewis Jones Laboratory, Freetown, Sierra Leone, West Africa; and T. SOUTHWELL, D.Sc., Ph.D., A.R.C. Sc., F.Z.S., F.R.S.E.; Lecturer in Helminthology, School of Tropical Medicine, Liverpool; formerly Director of Fisheries to the Government of Bengal, and Bihar and Orissa; Scientific Advisor and Inspector of Pearl Banks to the Ceylon Company of Pearl Fisheries; and Honorary Assistant, Zoological Survey of India. viii + 271 pages; 2 colored plates and 122 illustrations. William Wood and Company, New York, 1932. Price, $4.00.

A Guide to Human Parasitology is intended as a guide for a medical practitioner who has had no experience in the subject and the studies are made with such simple equipment as anyone practicing medicine could have at hand. Sources of material for practice are suggested and the importance of good preparations is stressed in these words, "the making of good blood or feces films is half the battle". The microscope and its use is explained in considerable detail, a point which scarcely seems necessary to the average present day medically trained person. Inspection of the table of contents at once reveals that the authors have arbi-

trarily limited the scope of their subject to the spirochetes and the animal parasites of man. This should be shown in the title as its present form is highly misleading. Are the pathogenic bacteria any less "parasitic" than the protozoa? More than half of the book is devoted to parasitic worms. Numerous charts and figures illustrate the diagnostic characters of the worms and their pathogenicity to man. The discussion of human trichinosis is inadequate for the needs of practitioners in this country. There is no mention of the cardiac complications, of the finding of larvae in the cerebrospinal fluid, or of the value of biopsy of muscle in doubtful cases. Clever "pictographs" are used to make clear the complete life history of the infecting organism. To the student these graphic presentations must prove of very great value. A few pages on myiasis follow. Near the end of the book is included an outline of treatment with a table of dosage for the diseases mentioned previously, and also a list of apparatus and chemicals needed in the study of parasites. This Guide is worth reading and will be useful to anyone particularly interested in parasitic worms. The charts and illustrations, particularly the "pictographs," add much to this book. Whether treatment should be taken up in such a brief manner is a question.

R. C. W.

A Handbook of Experimental Pathology. By GEORGE WAGONER, M.D., Associate in Pathology, and R. PHILIP CUSTER, M.D., Associate in Research Medicine, The School of Medicine, University of Pennsylvania. Foreword by Professor EDWARD BELL KRUMBHAAR. Illustrations by ERWIN F. FABER. xv+160 pages, 22 illustrations. Charles C. Thomas, Springfield, Illinois, 1932. Price, $4.00 postpaid.

A handbook dealing with the materials and methods of experimental pathology is timely for its aids in steering a course between utter neglect of this important aid to the study of the nature of disease on the one hand and ill-advised experimentation on the other. Throughout, care is taken to give methods which cannot be subject to deserved criticism as inhumane. After a very useful section on the housing and management of animals, technical methods are described in a general way and tables of normal blood findings in laboratory animals are provided. More than one hundred experiments in general and special pathology are described with stimulating questions and selected references for most of them. The illustrations of apparatus serve their purpose, but those showing the microscopical appearances of tissues are unsatisfactory. This book, the outgrowth of five years' experience, will prove a useful guide to teachers and students seeking to develop a dynamic conception of the processes of disease in the living body.

Diseases of the Thyroid Gland with Special Reference to Thyrotoxicosis. By CECIL A. JOLL, M.S., B.Sc. (Lond), F.R.C.S. (Eng.); Senior Surgeon to the Royal Free Hospital and the Miller General Hospital; Surgeon to the Cancer Hospital; Consulting Surgeon to the Royal Buckinghamshire Hospital; Late Hunterian Professor, Royal College of Surgeons. xviii+682 pages, 284 text figures, 24 colored plates. C. V. Mosby Company, St. Louis, Missouri, 1932. Price $20.00.

One wonders, in advance of examination of the book, at the temerity of the American distributors of this very expensive English text on diseases of the thyroid. Have we not felt that we have kept a little ahead of our colleagues in Great Britain in this very field of investigation? Close scrutiny of the book itself explains the venture. Although we may differ with the author on various questions, and particularly regret that he has not given fuller consideration to the constitutional pathology of Graves' disease, we recognize in Joll's treatise an orderly and well digested compilation of a huge material. Lack of recognition of the probable significance of lymphoid tissue in the thyroid is revealed by a glance at figure 12 which is labeled "normal thyroid gland" although it shows a "lymphorrhage". The acceptance of the conception of lymphadenoid goiter has similar significance. Critical analysis of the many chapters is impossible here. The numerous illustrations and particularly the fine

colored plates explain the relatively high cost of this volume. As an important reference book this monograph should be in every medical library and at the disposal of all who are especially concerned with diseases of the thyroid gland.

Oral Spirochetes and Related Organisms in Fuso-Spirochetal Disease. By DAVID T. SMITH, A.B., M.D., Associate Professor of Medicine, Duke University, School of Medicine, Durham, N. C.; formerly Bacteriologist and Pathologist to the New York State Hospital for Incipient Tuberculosis, Ray Brook, N. Y. xii+243 pages; 53 illustrations. The Williams and Wilkins Company, Baltimore, 1932. Price, $4.50.

"There is no evidence either clinical or experimental that the oral spirochetes alone can produce disease in man. But they are probably the most important member in a symbiotic group of anaërobic organisms which is capable of initiating a severe and often fatal disease. The first five chapters of this book deal with the biological characteristics of the mouth organisms. These are followed by presentation of the clinical aspects of the morbid states with which the fuso-spirochetal complex is associated. These are grouped by regions. While reference to the association of these conditions, and particularly the anginal group, with various pathological states of the blood is made, it would seem to be timely to give more emphasis and attention to the problem of granulocytopenia. Numerous historical references add interest; treatment is adequately considered, and a bibliography of 822 items (but without titles) brings this excellent monograph to a close. It is an important and useful text for clinicians, pathologists and laboratory workers.

An Introduction to Dermatology. By RICHARD L. SUTTON, M.D., Sc.D., LL.D., F.R.S. (Edin.), Professor of Diseases of the Skin, University of Kansas School of Medicine; and RICHARD L. SUTTON, Jr., A.M., M.D., Visiting Dermatologist to the Kansas City General Hospital. xvi+565 pages, 183 illustrations. The C. V. Mosby Company, St. Louis, 1932. Price $5.00.

This abridged text in dermatology is based on the eighth edition of *Diseases of the Skin* by the senior author. It is intended primarily for the student, and gives him the essential material requisite for his knowledge without that huge mass of information found in the larger texts, much of which is useful only to the specialist. The abridgement has been accomplished, not by the omission of diseases, but by reducing the general descriptions, the discussions, and statistical material. The illustrations are very well selected for their value in differential diagnosis, and are well reproduced. The book has a certain freshness of style and directness of approach which commend it most strongly. It should prove of great value to the practitioner as well as to the medical student

Diabetes in Childhood and Adolescence. By PRISCILLA WHITE, M.D., F.A.C.P., Physician at the New England Deaconess Hospital, Boston, Massachusetts. With a Foreword by ELLIOTT P. JOSLIN, M.D., F.A.C.P., Clinical Professor of Medicine, Harvard Medical School; Consulting Physician, Boston City Hospital; Physician at the New England Deaconess Hospital, Boston, Massachusetts. xiv+236 pages, 25 engravings and a colored plate. Lea & Febiger, Philadelphia, 1932. Price, $3.75.

Over 500 living cases of diabetes in the juvenile age period formed the basis of the material in this book. Throughout, the thesis is developed that the *living* diabetic child is the most outstanding medical accomplishment of the past decade. From nearly 100 per cent the mortality of diabetes in childhood has dropped nearly to the vanishing point. All phases of diabetes and of the physiology of the diabetic child are considered. The treatment of the disease itself and of its common complications is fully set forth. Not the least interesting is the chapter giving the present physiological, economic and social status of 76 diabetic children who have survived ten or more years. This book deserves a sympathetic reception and careful study. It reflects energetic study, achievement of a high order, and optimism.

A Text-book of Pathology. By W. G. MacCallum, Professor of Pathology and Bacteriology, The Johns Hopkins University, Baltimore. Fifth edition, thoroughly revised. xvi+1212 pages, 652 illustrations, many in color. W. B. Saunders Company, Phiadelphia and London, 1932. Price, $10.00.

A new edition of MacCallum's well-known textbook requires no introduction nor any explanation of its worth. Well-written, well-illustrated and well-printed, this work has been maintained at a high level of excellence by frequent revisions. For student and clinician alike it continues to provide a highly satisfactory foundation in the principles of general and special pathology. "A constant effort has been made to speak of the disturbances of function and of chemical interchange in the course of disease, as far as that was possible, and even to describe symptoms. If this makes the book seem like a treatise on clinical medicine, it is only because pathology and clinical medicine are, after all, the same thing viewed from slightly different angles."

The Sputum: Its Examination and Clinical Significance. By Randall Clifford, M.D., F.A.C.P., Associate in Medicine, Peter Bent Brigham Hospital; Assistant in Medicine, Harvard Medical School; formerly Associate Physician and Director of Pulmonary Clinic, Massachusetts General Hospital. xx+167 pages, 21 text figures and 7 plates in colors. The MacMillan Company, New York City, 1932. Price, $4.00.

Clifford's book is a complete practical guide to the collection and study of the sputum. Macroscopic and microscopic features, technical methods of examination, and methods of disinfection of the contents of the sputum cup are given in satisfactory detail. About fifty pages are devoted to a discussion of the character and clinical significance of the sputum in some twenty of the more common diseases of the bronchi and lungs. Both the black and white figures and the colored plates are well chosen and well reproduced. This book can be confidently recommended to students and practitioners.

Die Ernährung des Herzens und die Folgen ihrer Störung. [*The Nutritional Mechanism of the Heart, and the Results of Interference with It.*] Ergebnisse der Kreislaufforschung, Band III. By Dr. Med. Luigi Condorelli, Professor in the University of Naples. xii+230 pages, 70 illustrations, in part colored. Theodor Steinkopff, Dresden and Leipzig. 1932. Price, in paper, R M 18.80; bound, R M 20.00.

This monograph is divided into four major parts. The first describes in full the anatomy of the coronary circulation and of the lymphatics of the heart. In the second there is a broad treatment of the physiology of the vessels of the heart, including the effects of various drugs. The third chapter deals with the experimental pathology of the coronary system. In this section is included much original work by the author on modifications in the electrocardiogram following infarction of known areas in the myocardium. The final division presents the pathology in man associated with coronary disease, including the less well known forms of coronary arteritis. Each section has an extensive bibliography.

Experimental Pharmacology and Toxicology: A Selected Laboratory Course. By Henry G. Barbour, A.B., M.D., Yale University, New Haven, Connecticut. 141 pages, 14 illustrations. Lea & Febiger, Philadelphia, 1932. Price, $2.75, net.

Barbour's manual presents a selected laboratory course in pharmacology based on twenty years of experience. Naturally, its field of interest will be found to be largely restricted to teachers of this subject. It is a neat, well printed book, interleaved in blank for the taking of notes, and presents more than forty well chosen experiments.

Annual Report of the Surgeon General of the Public Health Service of the United States for the Fiscal Year 1932. vi + 199 pages.

United States Government Printing Office, 1932. For sale by the Superintendent of Documents, Washington, D.C. (Treasury Department Document No. 5053). Price, $1.00 (cloth).

College News Notes

AMENDMENTS TO THE BY-LAWS

The Board of Regents of the American College of Physicians submits herewith recommended amendments to the By-Laws, to be acted upon by the Fellows and Masters at the next Annual Business Meeting, Montreal, February 9, 1933.

The purposes of these amendments are:

1. To make the Editor of the official journal of the College an *ex officio* member of the Board of Regents;
2. To provide for a single Committee on Credentials, consisting of three appointees from the Board of Regents and three appointees from the Board of Governors, in order to promote unity in the application of admission standards and in order to simplify the procedure for the election of Associates.

It is, therefore, recommended that the following articles, or sections thereof, shall be amended to read as follows (italics indicate insertions or changes):

BY-LAWS, ARTICLE II, Section 1

"The Board of Regents shall consist of *twenty-four* members as follows: The President, the President-Elect, the Vice-Presidents, Secretary-General, Treasurer, Chairman of the Board of Governors, *Editor of the official journal,* and fifteen members elected from among the Masters and Fellows."

BY-LAWS, ARTICLE II, Section 4

"The Board of Regents shall appoint *three members to serve on the* Committee on Credentials whose duty it shall be to pass upon the qualifications of those proposed for Fellowship *or Associateship,* and recommend those considered eligible to the Board of Regents. *This Committee shall consist of six members, three appointed by the Board of Regents and three appointed by the Board of Governors, in such manner as to provide for continuity of service, with not more than one new member each year from each Board.*"

BY-LAWS, ARTICLE IV, Section 2

"The Board of Governors shall meet in executive session annually at the time and place of the annual meeting of the American College of Physicians for the transaction of such business as may come before it." (*Omit balance of paragraph.*)

BY-LAWS, ARTICLE IV, Section 6

"The Board of Governors shall appoint *three members to serve on the* Committee on Credentials whose duty it shall be to pass upon the qualifications of *those proposed for Fellowship or Associateship,* and recommend those considered eligible *to the Board of Regents.*"

BY-LAWS, ARTICLE V, Section 3 (c), paragraph 4

"The credentials of candidates for Fellowship shall be considered first by the Committee on Credentials, which Committee shall report to the Board of Regents for election, deferment or rejection."

BY-LAWS, ARTICLE VI, Section 2, sentence 2.

". . . . . After 1931, he may be required to present himself for personal examination, the character of which shall be determined by the Committee on Credentials."

"The credentials of candidates for Associateship shall be considered first by the Committee on Credentials, which Committee shall report to the Board of Regents for election, deferment or rejection."

BY-LAWS, ARTICLE VI, Section 3, paragraph 2, sentence 2

". . . . . At the expiration of three years, he shall be notified in writing by the Committee on Credentials of his eligibility for election to Fellowship during the next two years, provided he shall meet within that time the requirements necessary for Fellowship. If not elected to Fellowship within five years, his Associateship will automatically cease."

Respectfully submitted,

COMMITTEE ON CONSTITUTION
AND BY-LAWS
Sydney R. Miller, Chairman
Alfred Stengel
S. Marx White

Abstracts of Minutes of the Meeting of the

BOARD OF REGENTS

Philadelphia, Pa.
November 13, 1932

The Board of Regents of the American College of Physicians met at the College Headquarters in Philadelphia at 11:00 A.M., November 13, and was presided over by Dr. F. M. Pottenger, President.

Those present included Dr. F. M. Pottenger, Dr. George Morris Piersol, Dr. Maurice C. Pincoffs, Dr. Charles G. Jennings, Dr. William D. Stroud, Dr. William Gerry Morgan, Dr. Walter L. Bierring, Dr. George E. Brown, Dr. John H. Musser, Dr. O. H. Perry Pepper, Dr. James S. McLester, Dr. Jonathan C. Meakins, Dr. James H. Means, Dr. James Alex. Miller, Dr. Sydney R. Miller, Dr. David P. Barr, Dr. James B. Herrick, Dr. Clement R. Jones, Dr. S. Marx White and Dr. W. Blair Stewart. Dr. Charles H. Cocke, Dr. Ernest B. Bradley, members of the Committee on Credentials, and Dr. Alfred Stengel and Dr. Charles F. Martin, members of special Committees, were present as guests. The Executive Secretary, Mr. E. R. Loveland, acted as Secretary of the meeting.

The Executive Secretary read abstracted minutes of the meetings of the Board of Regents held at San Francisco, April 4-8.

The resignation of Dr. William Gerry Morgan, dated April 7, 1932, as a member of the Board of Governors was read, and upon motion regularly adopted, the resignation was accepted, in view of the fact that Dr. Morgan is now the Secretary-General of the College.

Eighteen special cases of members of the College, concerning illness, inability to pay dues, change of status, etc., were reviewed by the Secretary-General, Dr. Morgan, and individual action taken.

The resignations of five Fellows and two Associates were read by the Executive Secretary, and discussed by the Regents. Upon motion by Dr. McLester, seconded by Dr. Bierring, and regularly adopted, it was

RESOLVED, that action on the resignations of the members named be postponed until the Montreal meeting in view of the fact that the dues of the College are to be reduced and some of these members may desire to continue their memberships.

The Executive Secretary announced the following deaths, which had been reported since the last meeting of the Board of Regents:

Fellows:

Byron Fuller Barker, Bath, Maine ..... April 29, 1932
Ray Carrington Blankinship, Madison, Wis. ..... August 23, 1932
A. J. Burridge, Winnipeg, Man. ..... March 15, 1932
Luther C. Davis, Fairmont, W. Va. ..... September 5, 1932
Charles Joseph Durand, Colfax, Calif. ..... July 6, 1932
Elmer H. Funk, Philadelphia, Pa. ..... May 13, 1932

Alfred Leftwich Gray, Richmond, Va. ..... October 13, 1932
William C. Heussy, Seattle, Washington ..... March 21, 1932
John A. Lichty, Clifton Springs, N.Y. ..... May 2, 1932
Charles G. Lucas, Louisville, Ky. ..... July 7, 1932
Frederick Wilmot Mann, Houlton, Maine ..... June 16, 1932
Orlando H. Petty, Philadelphia, Pa ..... June 2, 1932
James Manara Rector, Columbus, Ohio ..... September 17, 1932
Lorraine Schwartz, Pittsburgh, Pa. ..... July 25, 1932
Benjamin F. Shuttleworth, Clarksburg, W. Va. ..... March 31, 1932
Leonard F. C. Wendt, Detroit, Mich. ..... June 11, 1932

Associates:

Edwin Massie Bell, Allenwood, Pa. ..... August 20, 1932
Charles Rollin Grandy, Norfolk, Va. ..... June 10, 1932
Aexander B. Kalbaugh, Westernport, Md. ..... May 15, 1932
Joseph W. Malone, Brooklyn, N.Y. ..... September 10, 1932
George Henry Sherman, Detroit, Mich. ..... April 19, 1932

On motion by Dr. White, seconded by Dr. James Alex. Miller, it was

RESOLVED, that the Secretary-General shall prepare appropriate resolutions for Dr. John A. Lichty, Dr. Charles G. Lucas and Dr. Elmer H. Funk, as past members of the Board of Regents, said resolutions to be submitted at the next meeting of the Board of Regents.

Letters by Dr. William J. Kerr, Dr. J. N. Hall, Dr. G. Gill Richards, Dr. James R. Arneill and Dr. C. T. Burnett, concerning the time of our Annual Clinical Sessions with regard to date were presented. A resolution was adopted that these letters be received.

Dr. E. A. Broughton, of Toronto, and Dr. Harold E. Waxman, of Pittsburgh, were reinstated as a Fellow and an Associate, respectively.

The following candidates were regularly elected to Fellowship in the College:

Anderson, Edward Waldemar ....Des Moines, Iowa
Cecil, Russell L. .....New York, N.Y.
Fort, Wetherbee .....Baltimore, Md.
Fox, Leon Alexander .....Washington, D.C.
French, Harry T. .....Hanover, N.H.
Gottlieb, Julius .....Lewistown, Maine
Hamilton, James .....Providence, R.I.
Hamilton, John Richard .....Nassawadox, Va.
Kolmer, John Albert .....Philadelphia, Pa.
Riven, Samuel Saul .....Nashville, Tenn.
Schoenheit, Edward William .....Asheville, N.C.
Swann, Walter Clifford .....Huntington, W. Va.

The Executive Secretary was requested to report upon the financial operation of the College for the current year. He presented the comparative cost analyses of the ANNALS OF INTERNAL MEDICINE for Volumes III, IV and V, showing a great improvement in the financial status of Volume V over Volume IV, due to a reduction in the volume of the News Notes Section, due to an increase in circulation, and due to a reduction in printing cost. He pointed out, too, that his office has been able to maintain, in fact slightly to increase, the amount of paid advertising in the journal over previous years, in spite of the financial situation. He then presented a comparative cost analysis for conducting the last four Clinical Sessions, this statement disclosing that the San Francisco Clinical Session for the current year cost $8,129.80 more than any previous Clinical Session, due to an increase in the traveling expenses of guest program speakers and members of the Board of Regents, and due, also, to certain increased local costs in San Francisco. In commenting on the other expenditures for 1932, he pointed out that the expenditures for his office had been reduced by securing a reduction of $240.00 in rental for the Executive Offices, and by a re-

duction in the office staff of a secretarial assistant whose salary was $1200.00 per annum. Other economies had also been put into effect, so that had we not had the increase in the cost of the San Francisco Clinical Session and the added expenses of the Phillips Memorial Prize, which in itself amounted to a total of $1878.82, which had not been granted in previous years, the surplus for 1932 would be approximately as large as for any preceding year, in spite of the fact that the income from initiation fees has been reduced at least fifty per cent. The application of the new provision of the By-Laws requiring all new members to come in first as Associates eliminates at this time the larger initiation fees paid in previous years, the shrinkage in income from this source alone for 1932 amounting to approximately $9000.00. It is estimated that there will be a surplus of income over expenditures at the end of 1932 of $5587.52. The Executive Secretary further asserted that the salaries of his office staff were not above the present level. In fact, that in the case of his Secretary, he considered her underpaid.

Dr. William D. Stroud presented the Treasurer's report, including the following bank balances as of October 31, 1932:

On deposit in closed banks:		
Bank of Pittsburgh	$ 7,797.16	
Exchange National Bank, Pittsburgh	3,887.12	
Highland National Bank, Pittsburgh	6,627.51	$ 18,311.79
On deposit in open accounts:		
Colonial Trust Company, Pittsburgh	7,398.86	
Commonwealth Trust Co., Pittsburgh	989.62	
First National Bank, Pittsburgh	2,486.83	
Girard Trust Co., Philadelphia	21,770.96	32,646.27
		$ 50,958.06

He recommended authorization by the Board of Regents to open an account in a Montreal bank for convenience in depositing Canadian checks and for the payment of Canadian bills during the period of the forthcoming Clinical Session. He further reported the elimination of practically all costs in conducting the Treasurer's office, since his assumption of the Treasurer's duties, due to the fact that he requires no secretarial assistance, such work being done in the Executive Secretary's office. His summarized report follows:

Endowment Fund, January 1, 1932		$ 52,400.00
General Fund, January 1, 1932		57,166.00
		$109,566.00
Income, January 1, 1932, to October 31, 1932	$ 39,563.17	
Expenditures, January 1, 1932, to October 31, 1932	29,370.65	
Excess income over expenses, October 31, 1932	$ 10,192.52	
Estimated expenses for November and December, 1932	4,605.00	5,587.52
This, plus Endowment Fund and General Fund of January 1, 1932, gives a total balance of		$115,153.52

Dr. Stroud further reported that two of the closed banks had paid dividends during the year, and that the ex-Treasurer, Dr. Jones, had expressed the opinion that the closed banks in Pittsburgh, in which balances of College funds remain, would eventually pay the College in full.

Dr. Clement R. Jones, Chairman of the Finance Committee, then presented his report, which was freely discussed by all present. In connection with expenses, Dr. James Alex. Miller inquired concerning a control of the expenses of the annual meetings, and was informed that the expenses of the Executive Secretary only were budgeted and limited, and that there had been no budget control or recommendations for the General Chairman,

local committees and the President. Dr. Miller recommended that when the meeting place for 1934 is selected, the Finance Committee shall prepare a budget for the General Chairman and for the President, limiting the expenditures that may be made.

The following resolution was regularly adopted

RESOLVED: (1) That the annual dues for Fellows shall be reduced to $15.00, and of Associates to $12.00, per annum, for the year 1933;

(2) That the Treasurer shall recommend to the Finance Committee an additional depository in Philadelphia and one in Montreal;

(3) That the securities of the College now held in Pittsburgh shall be transferred to a Philadelphia bank;

(4) That the John Phillips Memorial Prize for 1933 be in the sum of $1000.00, plus the expenses of the recipient to the Seventeenth Annual Clinical Session;

(5) That the Treasurer shall be authorized to purchase with approximately $1000.00, representing interest on securities now on deposit, a Government bond either of the United States or of Canada;

(6) That $50.00 per month for November and December shall be transferred from the Treasurer's budget for 1932 for the payment of secretarial services of the new Editor of the ANNALS OF INTERNAL MEDICINE, Dr. Maurice C. Pincoffs;

(7) That there be a temporary reduction in the salary of the Executive Secretary, of ten per cent as an estimated equivalent to the present reductions in costs of living, and that the matter of the reduction in the budget for his office staff be left to his discretion;

(8) That the salary of the Editor of the ANNALS OF INTERNAL MEDICINE be reduced ten per cent per annum;

(9) That the President-Elect be authorized to secure any appropriate reduction in rent;

(10) That the Finance Committee following the selection of the meeting place each year be instructed to prepare a budget for the President and the local General Chairman, controlling the expenses for their respective programs.

Dr. James H. Means, Chairman of the Committee on the John Phillips Memorial Prize, reported that in accordance with the regulations governing the award of the Phillips Memorial Prize, his Committee had selected a candidate for 1933 and presented the following resolution, which was duly seconded and regularly approved by the Board:

RESOLVED, that the John Phillips Memorial Prize for 1933 be awarded DR. WILLIAM B. CASTLE, of Boston, for his series of studies showing the relation of gastric digestion to the pathogenesis of anemia, the demonstration of the rôle of extrinsic and intrinsic factors in hematopoiesis, and finally in the demonstration that the extrinsic factor in treating pernicious anemia can be obtained from yeast as well as meat, suggesting that it is closely related to vitamin B.

Dr. Maurice C. Pincoffs, Chairman of the Committee on ANNALS OF INTERNAL MEDICINE, reported that the Executive Secretary had assembled estimates from ten different printers, including the Ann Arbor Press, for printing the ANNALS OF INTERNAL MEDICINE, and that the estimates submitted disclosed that material saving could be made during the coming year, either by continuing with the Ann Arbor Press, who had submitted a lower price than that at which they are now printing the journal, or by changing the printers. In view of the desirability of keeping the present volume with the same format, arrangement, etc., and, further, in view of the fact that going on with the present printers would be an aid to him in the formative period of his Editorship, Dr. Pincoffs wished to recommend that the Ann Arbor Press continue to print the journal up to and including the June, 1933, number. His Committee had further considered certain changes,

such as the elimination of abstracts and the enlargement of book reviews; also the matter of the size of the type page and various other details which they felt might somewhat improve the journal. Dr. Pincoffs asked for an expression of opinion by the Board as to the obligation to print every paper presented on the General Program of the Annual Clinical Sessions, expressing the feeling that he felt it was not desirable so to do, but that the Editor should have the same privilege of selection as he has with the acceptance of papers from those submitted directly.

The following resolution was regularly adopted:

RESOLVED, that it is the sense of the Board of Regents that a statement be sent to each essayist on the General Program that there is a requirement of the Board that their manuscripts be submitted in completed form at the time of delivery at the meeting for consideration for publication by the Editor of the ANNALS OF INTERNAL MEDICINE.

Dr. Sydney R. Miller, Chairman of the Committee on Constitution and By-Laws, reported that three matters had been referred to his Committee for consideration in regard to amendments to the By-Laws:

(1) The making of the Editor of the ANNALS OF INTERNAL MEDICINE an *ex officio* member of the Board of Regents instead of continuing a precedent of having the Editor continuously act as the First Vice-President of the College;

(2) An amendment to the By-Laws in regard to a resolution adopted by the Board of Regents on April 6, 1932, and referring to a provision for the appointment of a Finance Committee of three from the Board of Regents to perform certain duties;

(3) Advisability of amending the present provisions for two separate Committees on Credentials, and to provide for one Committee, consisting of three appointees from the Board of Regents and three appointees from the Board of Governors, with provision for the continuity of their service, and with an amendment to the By-Laws with respect to the method of election of Associates.

Dr. Miller reported that the first and third items, in their opinion, fully merited amendments to the By-Laws, but that the second item is unnecessary, since the present By-Laws, Article II, Section 3, fully provide that it is within the province and authority of the Board of Regents "to create, appoint and direct all standing Committees". His Committee recommended that the Board of Regents provide for a standing Committee of three members, appointed in such manner as to provide that one member shall retire each year, his vacancy being filled on appointment by the President, and that the Finance Committee shall be advisory, and its duties and powers defined from time to time by the Board of Regents.

RESOLVED, that the Board of Regents approves of the recommendations by the Committee on Constitution and By-Laws, and hereby instructs that Committee to prepare the detailed amendments and publication of same at least one month in advance of the next General Business Meeting in February.

Dr. Charles G. Jennings, Chairman of the Committee on Public Relations, reported the receipt of a number of communications asking for an investigation of the activities of Fellows of the College who are connected with certain groups, or clinics, which appear to be inconsistent with the ethical standards of the College. Cases also submitted dealt with group practice and contract medicine. The Committee recommended that the Board of Regents advise these correspondents that the College has no adequate method of determining the character of these criticized activities; and that the Board delay action upon them pending action by local medical bodies. The Committee on Public Relations further recommended that the Board of Regents suggest to the Committee on Credentials that it give full consideration to participation in these activities by applicants for membership in the College. The Committee considered, without formal action, questions in reference to abuses that may exist in the operation of the Veterans' Compensation Bureau and the Workingmen's Compensation Acts. Further information will be secured concerning the working of these bodies, in order that the Committee may be better prepared to consider them in the future. The report of the Committee was formally approved by the Board of Regents.

Doctors Pottenger and Meakins presented reports concerning the program for the Seventeenth Annual Clinical Session at Montreal.

Dr. James B. Herrick presented an invitation from all the grade A medical schools in Chicago, the Chicago Medical Society, the Illinois State Medical Society, the Chicago Association of Commerce, and the Mayor of Chicago, for the American College of Physicians to meet in the City of Chicago in 1934. The Board, as a body, expressed their appreciation of the invitation and assured Dr. Herrick that when the matter of the next meeting city is considered during the forthcoming Montreal Session, his invitation from Chicago will be most carefully considered.

The following resolution was regularly adopted:

RESOLVED, that the President appoint a member to fill the vacancy on the Committee on Credentials for Fellowship, due to the death of Dr. John A. Lichty.

President Pottenger announced the reappointment of Dr. W. Blair Stewart as a member of the Committee on Public Relations; his new term to terminate with the 1936 Session.

The following resolution was regularly adopted:

RESOLVED, that the President appoint Dr. James H. Means as the official delegate of the American College of Physicians to attend the International Goiter Conference at Berne, dependent upon the development of his plans to attend this Conference.

Adjournment.

At a recent meeting in Chicago, the directors of Alpha Omega Alpha Honor Medical Society adopted resolutions in recognition of the eminent services of the late Dr. William W. Root, Slaterville Springs, New York, the founder of the society and secretary-treasurer since its organization in 1902. The present officers of the society are Walter L. Bierring (Fellow), Des Moines, president; Austin A. Hayden, Chicago, vice-president; Josiah J. Moore (Fellow), Chicago, secretary-treasurer. Mrs. Root will continue as assistant secretary. In addition to the officers, the directorate includes Ray Lyman Wilbur, Washington, D.C.; Waller S. Leathers (Fellow), Nashville; Louis B. Wilson, Rochester, Minn., and Willard C. Rappleye (Fellow), New York City. The committee on extension and policy comprises Elias P. Lyon, Minneapolis, chairman; William Pepper, Philadelphia; Irving S. Cutter, Chicago; Frederick C. Waite, Cleveland, and Thomas C. Routley, Toronto.

Dr. Ray M. Balyeat (Fellow), Oklahoma City, addressed the 35th annual meeting of the Santa Fe Railway Medical and Surgical Society at Topeka, December 5, 1932, on "Allergic Diseases: With Special Reference to Symptoms Due to Allergy Simulating Surgical Conditions".

Dr. Herman B. Allyn (Fellow), Philadelphia, was made the guest of honor at the annual dinner of the Association of Ex-resident and Resident Physicians of the Philadelphia General Hospital, held at the Philadelphia Country Club on December 6, 1932. Dr. Allyn had been successively Interne, Registrar and Visiting Physician to the hospital, serving in all about thirty-five years. At the time of his retirement from active service he was President of the Medical Board of the Hospital. He is now Consulting Physician.

Doctor Wm. M. James (Fellow), Panama, is the author of two papers which have appeared in the Annual Report for 1931 of the Medical Department of the United Fruit Company. In this same volume there are also two papers by Doctor Ricardo Aguilar (Fellow), Quirigua, Guatemala; and a book review by Doctor Lawrence Getz (Fellow), Panama.

Doctor Julius Friedenwald (Fellow), Baltimore, has been elected President of the Baltimore City Medical Society for the year 1933-34.

Dr. David Riesman (Fellow), Philadelphia, delivered an address on "The Oldest Medical School in America" before the Society of the County of Kings in Brooklyn, New York, on December 20, 1932.

PROGRAM SEVENTEENTH ANNUAL CLINICAL SESSION OF THE AMERICAN COLLEGE OF PHYSICIANS

Montreal, Can., February 6-10, 1933

Francis M. Pottenger, President
General Sessions

Jonathan C. Meakins, General Chairman
Clinical Program

E. R. Loveland, Executive Secretary
133-135 South Thirty-sixth Street
Philadelphia, Pa.

GENERAL AND HOTEL HEADQUARTERS: WINDSOR HOTEL,

Dominion Square, Montreal, Can.

LIST OF MONTREAL HOTELS

All Prices Are for Rates per Day, European Plan

Windsor (Headquarters)	(Capacity 610)	
Single room without bath	$2.50	
Single room with bath	4.00	
Double room without bath	4.00	
Double room with bath	7.00	
Mount Royal	(Capacity 1050)	
Single room with bath	$3.00 up	
Double room with bath	6.00 up	
Ford	(Capacity 750)	
Single room without bath	$1.50 to	$2.00
Single room with bath	2.00 to	2.50
Double room without bath	3.00 to	3.50
Double room with bath	4.00 to	5.00
Queen's	(Capacity 350)	
Single room without bath	$2.00 to	$2.50
Single room with bath	3.00 to	4.00
Double room without bath	4.00 to	5.00
Double room with bath	6.00 to	8.00
Hotel De LaSalle	(Capacity 250)	
Single room with bath	$3.00 to	$6.00
Double room with bath	4.00 to	7.00
Ritz-Carlton	(Capacity 218)	
Single room with bath	$4.00 up	
Double room with bath	8.00 up	
Place Viger	(Capacity 118)	
Single room without bath	$2.50 to	$3.50
Single room with bath	3.50 to	5.00
Double room without bath	4.00 to	6.00
Double room with bath	7.00 to	10.00

WHO MAY REGISTER—

(a) All members of the American College of Physicians in good standing for 1933 (dues, if not paid previously, may be paid at the Registration Desk).

(b) All newly elected members.

(c) Members of the Montreal Medico-Chirurgical Society, La Société Médicale, Montreal Clinical Society, L'Association des Médecins du Nord, L'Association des Médecins del l'Est and L'Action Médicale, without registration fee, upon presentation of their 1933 membership cards.

(d) Medical students pursuing courses at McGill University and the University of Montreal, without registration fee, upon presentation of matriculation cards, or other evidence of registration at these institutions.

(e) House Officers of the hospitals participating in the program, upon presentation of proper identification.

(f) Members of the Medical Corps of Public Services of the United States and Canada, without registration fee, upon presentation of proper credentials.

(g) Qualified physicians who may wish to attend this Session as visitors. Such visiting guests shall pay a registration fee of $12.00, and shall be entitled to one year's subscription to "Annals of Internal Medicine" (in which the proceedings will be published), included within such fee.

REGISTRATION BUREAU.—Located in the Rose Room, Windsor Hotel. Hours: 8:00 A.M. to 6:00 P.M., daily, February 6-10.

REGISTRATION BLANKS FOR ALL CLINICS AND DEMONSTRATIONS are sent to members with the official program. Guests will secure registration blanks at the Registration Bureau during the Session.

TRANSPORTATION—A reduction to one and one-half fare for the round trip on the "Identification Certificate Plan" will apply for physicians and dependent members of their families.

Members are privileged to make the going journey by one route and return by another route. The fare for children of five and under twelve years of age will be one-half of the round trip fare for adults; children under five years of age free when accompanied by parents or guardian. Stop-overs will be allowed at all stations within final limit on either going or return trip, or both, on application to conductors.

Before purchasing tickets, members must secure from the Executive Secretary an Identification Certificate, to entitle them to the reduced fares.

In general, tickets will be sold from January 28 to February 10, depending upon the relative distance from Montreal, with a return limit of thirty days in addition to date of sale.

All tickets must be validated by a special railroad agent at the Montreal headquarters from February 6-10.

BANKING FACILITIES

Arrangements have been made with the *Royal Bank of Canada* to exchange money and cash cheques for the registered visitors to the Clinical Session. The Bank has made these special arrangements in their Branch at the corner of St. Catherine and Stanley Streets, which is two blocks removed from the Headquarters in the Windsor Hotel.

THE GENERAL BUSINESS MEETING OF THE COLLEGE will be held at 4:30 P.M., Thursday, February 9, immediately following the general scientific program of the afternoon. All Masters and Fellows of the College are urged to be present.

There will be the election of Officers, Regents and Governors, the reports of the Treasurer and of the Executive Secretary and the induction to office of the new President, Dr. George Morris Piersol, Philadelphia, Pa.

SPECIAL FEATURES

Monday, February 6, 1933

The John Phillips Memorial Oration will be delivered by Dr. William B. Castle, of Boston, Mass., at the evening General Session at 9 o'clock. After this a *Smoker* will be held in the Prince of Wales Salon of the Windsor Hotel. There will be a program of entertainment, and refreshments will be served. Members of the College, guests and visitors are cordially invited to attend, as it is hoped that this informal function will provide an opportunity early in the Session for members and guests to meet each other.

Tuesday, February 7, 1933

A Hockey Match between "The Canadiens" of Montreal and "The Maple Leafs" of Toronto, in the National Hockey League, will be played at the *Forum* (corner of St. Catherine Street and Atwater Avenue) at 8:00 P.M. A block of seats has been reserved for the Fellows and visitors, and tickets may be obtained at the Information or Registration Bureaus before 1:00 P.M., Tuesday.

Wednesday, February 8, 1933

CONVOCATION OF THE COLLEGE—8:00 o'clock, Windsor Hall. All Masters and Fellows of the College and those to be received in Fellowship should be present. Newly elected Fellows who have not yet been received in Fellowship are requested to occupy the central section of seats especially reserved for them. As this is the most formal meeting of the College, it is urged that all appear in evening dress.

The Convocation is open to all physicians and their families generally, and to such of the general public as may be interested.

Following the Convocation Ceremony, the President of the College will present the John Phillips Memorial Prize for 1933 to Dr. William B. Castle, of Boston, Mass.

Sir Andrew MacPhail, Professor of the History of Medicine, McGill University, will deliver an address on "The Source of Modern Medicine."

The President, Dr. Francis M. Pottenger, of Monrovia, Calif., will then deliver the annual presidential address to the Masters, Fellows and Associates of the College.

The Presidential Reception will follow immediately after the program. Newly inducted Fellows should sign the Roster and secure their Fellowship Certificates during the interim between the Convocation and the Reception.

Thursday, February 9, 1933

THE ANNUAL BANQUET OF THE COLLEGE will be held at the Windsor Hotel at 7:30 P.M. All members of the College and its Officers, physicians of Montreal and visitors attending the Session, with their wives, are invited to be present at the Banquet.

Dr. Charles F. Martin will act as Toastmaster, and Dr. Stephen Leacock, William Dow Professor of Political Economy, McGill University, will deliver an address on "The Waste Spaces of Modern Education."

Tickets for the Banquet, $5.00 per person, may be purchased at the Registration or Information Bureaus before 10:00 A.M., Thursday.

ENTERTAINMENT FOR VISITING WOMEN

A program has been arranged for the entertainment of the visiting women in attendance at the meeting, but ample time has also been allowed for individual excursions and shopping. Shopping lists, including the names of the principal shops, will be issued by the Local Committee for the Entertainment of Visiting Women.

POST-CONVENTION TOURS

In order that those attending the Session may have an opportunity of visiting historic Quebec City in its splendid winter garb and enjoy the winter sports, the railways will offer reduced week-end rates. In addition, the Chateau Frontenac Hotel, so beautifully situated

on the bold cliff overlooking the city and river, is making a special rate of seven dollars ($7.00) a day, American Plan, for any who may wish to visit Quebec City on a post-convention trip.

Similar arrangements have been made with the Seigniory Club at Lucerne-in-Quebec for the rate of eight dollars ($8.00) a day, American Plan. The Seigniory Club, Lucerne-in-Quebec, is built around one of the old French-Canadian seigneuries with buildings including the old Manor House, the Log Chateau (with accommodation for 300 members and guests), a year-round swimming pool and sports Club House. It is situated in the Laurentian Mountains, seventy-five miles from Montreal.

THE EXPOSITION AND COMMERCIAL EXHIBIT will be located in the Concourse and Rose Room of the Windsor Hotel, in close proximity to Windsor Hall, the meeting hall for the General Sessions.

Exhibits, consisting of medical literature and texts, pharmaceutical products, apparatus and appliances, special foods, etc., will be shown by leading American and Canadian publishers and manufacturers. These exhibits afford an opportunity for physicians to examine the latest literature and the newest products in the field of medicine generally; their educational value should not be overlooked. Every attendant at the Session is urged to visit each of the booths, for he cannot help but find something new, interesting and scientifically valuable. Intermissions in the general program have been arranged from Tuesday to Friday, inclusive, for the purpose of providing a definite time for the inspection of exhibits.

CLINICAL PROGRAM

Full advantage has been taken of the excellent facilities for clinical teaching which are afforded by the hospitals attached to the two Medical Schools in Montreal. It has been found possible to provide ample accommodation for the Clinical Session in eight places which are practically all within a short distance of the Headquarters. They consist of four large general hospitals, two pediatric hospitals, and the Biological Building, Pathological Institute, and Medical Building of McGill University. Daily bedside and theatre clinics have been arranged in all of these hospitals and demonstrations in the University buildings.

Medical Libraries—The Medical Library of McGill Medical School and the Osler Library, the gift of the late Sir William Osler, will be open to visitors daily, both morning and afternoon. There will be found in both a large collection of medical books, both ancient and modern. All who are interested in rare editions are advised to pay these libraries a visit.

Medical Museums—The Medical School of McGill University has for several generations been very rich in its museum collections. These are now housed at the McGill Medical Building and also at the Pathological Institute.

Special exhibits of "Congenital Heart Disease," Sir William Osler's collection of pathological specimens with their biographies which he compiled during his period as Pathologist at the Montreal General Hospital, and a collection illustrative of Medical History covering many parts of the world, will be arranged for daily inspection by the Fellows and visitors.

DEMONSTRATIONS AT THE McGILL MEDICAL BUILDINGS

Demonstrations have been arranged in the laboratories of the Departments of Pharmacology, Biology, Physiology and Anatomy. These will cover the special work that is occupying the attention of these various departments and should interest many of the Fellows and visitors.

Clinico-pathological Conferences will be held each morning at the Montreal General Hospital. These conferences have been held for many years and hold a unique position in the medical activities of this institution.

At the Royal Victoria Hospital Professor Oertel will conduct the Conference, on Thursday morning. On the other mornings there will be demonstrations by the Staff of the Pathological Institute dealing with a variety of pathological subjects.

EXPERIMENTAL MEDICINE

In the laboratories of the University Clinic at the Royal Victoria Hospital there will be demonstrated each morning at 11 o'clock interesting results in various problems of Medicine.

PEDIATRICS

A varied program for those interested in Pediatrics has been provided at both the Children's Memorial Hospital and the Hôpital Ste. Justine. The symposia at the former institution on lead poisoning and rheumatic fever in childhood should be particularly attractive.

PSYCHIATRY AND NEUROLOGY

In addition to a number of clinics on neurological subjects, there have been arranged two symposia. One deals with the influence of emotional factors in organic disease, while the other is devoted to the problem of epilepsy.

GENERAL CLINICS

Many clinics have been arranged in cardiovascular, gastro-intestinal, pulmonary, and blood diseases, as well as diseases of the ductless glands and of metabolism.

There will be clinical symposia on diseases of the biliary passages, diabetes, goitre, collapse therapy in pulmonary tuberculosis, syphilitic cardiovascular disease, nephritis, and essential hypertension.

In addition to the small bedside clinics, larger ward clinics have been arranged by the Senior Members of the Staff at the Montreal General Hospital. At the Royal Victoria Hospital one ward has been set aside each day for the demonstration of interesting cases. The Fellows and visitors are invited to visit these wards at their leisure when they may examine and discuss the problems they present with members of the Staff.

GENERAL SESSIONS

In preparing the program for the General Sessions we have attempted to make it reflect the best work that is being done in medicine. The place which the College holds in the minds of medical men can well be estimated from the ready response of those invited to present papers. The response on the part of those who were able to attend the meetings was almost 100 per cent. While the contributors come from various parts of the country it was necessary in constructing the program this year to bear in mind the deterrent effect of long journeys.

There are several features of the program which require emphasis.

That physiological studies are coming more and more to the fore in medical work will be emphasized by the fact that there is a thread of physiology both normal and pathological running through most of the discussions in this program.

Constitutional factors of both an anatomical and physiologic nature will be discussed. The physiological activity of the cell will be presented from both a theoretical and practical standpoint. The difference in chemical constitution favorable to various diseases and the manner in which diseases may be influenced by altering body chemistry will be dwelt upon.

The place of the two correlating mechanisms of the body—the chemical in the form of hormones, and the nervous as represented by both the somatic and visceral nervous systems—is discussed, and the relationship of these systems to normal and pathological function will be stressed.

Endocrinology—A special feature is the symposium on endocrinology, in which the papers will be presented by investigators to whom we are indebted for original work in the particular field discussed. With the new work which is being brought out in this field many of the enigmas of metabolism, growth and development are now being solved, and the body reactions heretofore inexplicable are now being understood.

The Nervous System—Neurology and the psychical side of medicine will be stressed in several important papers dealing with problems of both an organic and functional nature. Epilepsy and schizophrenia will be treated from special standpoints. The part which the autonomic nervous system plays in disease will be presented in practical form.

Pulmonary diseases will be discussed from several angles. Tuberculosis will be presented from the standpoint of the internist as well as the specialist. The suppurative lesions of the chest will be presented by our distinguished French guest and by America's pioneer chest surgeon. The lung will also be discussed from the standpoint of being a focus of systemic infection.

The Heart and Arterial System hold the attention of medical men in a special manner, because of their increased morbidity now that so large a percentage of people are living beyond middle life. Angina pectoris will be treated from both the medical and surgical aspects. Papers on electrocardiography, endocarditis, valvular lesions, the effect of hyperthyroidism on the heart and pulsus alternans will be presented.

Lesions of the peripheral vascular system will be presented. The fact that these affections have recently been treated more or less successfully by operative procedure, based on a better understanding of vascular neurology, adds an ever increasing interest to the subject.

Miscellaneous Subjects—The rôle which sensitization plays in immunity is an important and fascinating subject, and will be presented in an authoritative manner. There will also be discussions of the so-called allergic diseases, diabetes, diseases of the blood, diseases of the pancreas and liver, neurosyphilis, and other problems which are met daily by clinicians. The history and philosophy of medicine will be presented by a paper on the Source of Modern Medicine.

The John Phillips Memorial Prize Oration will be given on Monday evening by William B. Castle, of Boston, for his series of studies showing the relationship of gastric digestion to the pathogenesis of anemia, the demonstration of the rôle of extrinsic and intrinsic factors in hematopoiesis, and finally in the demonstration that the extrinsic factor beneficial in pernicious anemia can be obtained from yeast as well as meat suggesting that it is closely related to Vitamin B.

Through the courtesy of the Provincial Government we are especially fortunate in having a distinguished Parisian physician participate in our program.

OPENING GENERAL SESSION

Monday Afternoon, February 6, 1933
2:00 o'Clock

WINDSOR HALL

1. Addresses of Welcome:
   The Honourable L. A. Taschereau, K.C., Premier of the Province of Quebec.
   The Honourable Fernand Rinfret, Mayor, City of Montreal.
   Charles F. Martin,† Dean, Faculty of Medicine, McGill University.
   L. de L. Harwood, Dean, Faculté de Médecin, Université de Montréal.
2. Response to Addresses of Welcome:
   F. M. Pottenger,* President of the American College of Physicians.
3. The Diagnostic Use of Iodine in Thyrotoxicosis.
   James H. Means,* Boston, Mass.
4. Irradiation Treatment of Hyperthyroidism.
   George E. Pfahler,* Philadelphia, Pa.
5. Some Aspects in Cell Physiology.
   W. J. V. Osterhout, New York, N.Y.
   (Guest)
6. The Effect of Vitamins and the Morgonic Elements on the Growth and Resistance to Disease in Children.
   Alan Brown, Toronto, Ont.
   (Guest)

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†M.A.C.P. *F.A.C.P.

7. A Study of the Ultra Violet Rays in the Western and Southwestern Portions of the United States.
Meldrum K. Wylder,* Albuquerque, N.M.

SECOND GENERAL SESSION
Monday Evening, February 6, 1933
8:00 o'Clock
WINDSOR HALL

1. Spontaneous Versus Artificial Regulation of Constitution for the Control and Prevention of Disease.
Millard Smith, Boston, Mass.
(Guest)
2. The Rôle of Desensitization in Recovery from Bacterial Infections.
William B. Wherry, Cincinnati, Ohio.
(Guest)

9:00 o'Clock

JOHN PHILLIPS MEMORIAL PRIZE ORATION
"The Etiology of Pernicious Anemia and Related Macrocytic Anemias."
William B. Castle,* Boston, Mass.

10:00 o'Clock

SMOKER
Prince of Wales Salon

THIRD GENERAL SESSION
Tuesday Afternoon, February 7, 1933
2:00 o'Clock
WINDSOR HALL
Presiding Officer
Jonathan C. Meakins,* Montreal, Que.

1. Treatment of Polycythemia Vera.
Ernest Falconer,* San Francisco, Calif.
2. Polycythemia Associated with Pulmonary Disorders
James J. Waring* and W. B. Yegge,* Denver, Colo.
3. The Platelets and Platelet Volume in Blood Dyscrasias.
H. Z. Giffin* and K. K. Nygaard, Rochester, Minn.
4. Observations on Addisin in Diseases of the Blood.
Roger S. Morris,* Cincinnati, Ohio.
5. Anatomy and Physiology of the Cerebral Circulation.
Stanley Cobb, Boston, Mass.
(Guest)
6. The Patient as a Person.
A. H. Gordon, Montreal, Que.
(Guest)
7. The Influence of Diets High in Fat upon the Insulin Treated Cases of Diabetes.
Henry Rawle Geyelin, New York, N.Y.
(Guest)
8. Lower Fat Diet in Diabetes.
Joseph H. Barach,* Pittsburgh, Pa.

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*F.A.C.P.

9. Complications of Diabetes.
   Lea A. Riely,* Oklahoma City, Okla.
10. Gastro-intestinal Allergy in Children.
   Horton Casparis,* Nashville, Tenn.
11. Clinical Observations on Some of the Causes, Organic and Other, of Abdominal Pain and Distress.
   S. Franklin Adams,* New York, N.Y.

FOURTH GENERAL SESSION

Tuesday Evening, February 7, 1933
8:00 o'Clock

WINDSOR HALL
Presiding Officer
David Preswick Barr,* St. Louis, Mo.

1. Carbohydrate and Fat Metabolism.
   C. H. Best, Toronto, Ont.
   (Guest)
2. The Biochemistry and Physiology of the Follicular Hormone.
   E. A. Doisy, St. Louis, Mo.
   (Guest)
3. Studies on the Function and Clinical Use of Cortin.
   Frank A. Hartman, Buffalo, N.Y.
   (Guest)
4. Physiology of the Anterior Pituitary and Relationship of Pituitary to Placental Hormones.
   J. B. Collip, Montreal, Que.
   (Guest)
5. Therapeutic Use of Placental Hormones.
   A. D. Campbell, Montreal, Que.
   (Guest)
6. Differentiating the Functions of the Anterior Pituitary Hormones.
   Oscar Riddle, Cold Spring Harbor, L.I., N.Y.
   (Guest)
7. Effect of Hormones on Cellular Permeability.
   Ernest Gellhorn, Chicago, Ill.
   (Guest)

FIFTH GENERAL SESSION

Wednesday Afternoon, February 8, 1933
2:00 o'Clock

WINDSOR HALL
Presiding Officer
James Alex. Miller,* New York, N.Y.

1. Pulmonary Tuberculosis in General Practice.
   Reginald Fitz, Boston, Mass.
   (Guest)
2. Conservatism the Keynote in the Treatment of Tuberculosis.
   Charles H. Cocke,* Asheville, N.C.
3. The Indications for Collapse Therapy in Pulmonary Tuberculosis.
   Isidor David Bronfin,* Denver, Colo.

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*F.A.C.P.

4. Reflections Concerning the Treatment of Chronic Purulent Bronchiectasis.
   Edward W. Archibald, Montreal, Que.
   (Guest)
5. Collapse Therapy of Bronchiectasis.
   E. Rist, Paris, France.
   (Guest)
6. The Rheumatic Lung.
   C. P. Howard, Montreal, Que.
   (Guest)
7. Hereditary Abnormalities and Constitutional Traits in Experimental Animals.
   Wade H. Brown, New York, N.Y.
   (Guest)
8. The Value of the Galactose Test in the Diagnosis and Prognosis of Intrahepatic Icterus.
   George Morris Piersol,* Philadelphia, Pa.
9. The Differential Diagnosis of Diseases of the Liver and Spleen by the Aid of Roentgenography after Intravenous Injection of Thorium Dioxide Sol.
   Wallace M. Yater,* Washington, D.C.
10. Some Clinical Aspects of the Acid Base Balance of the Body.
    Samuel M. Alter,* Los Angeles, Calif.
11. Radiotherm Therapy in Neurosyphilis.
    Walter M. Simpson,* Dayton, Ohio.

ANNUAL CONVOCATION

Wednesday Evening, 8:00 o'Clock

WINDSOR HALL

The general profession and the general public are cordially invited. No special admission tickets are required. Evening dress is recommended.

1. Convocation Ceremony.
2. Address: "The Source of Modern Medicine."
   Sir Andrew MacPhail, Montreal, Que.
3. Presentation of the John Phillips Memorial Prize.
4. President's Address.
   F. M. Pottenger, Monrovia, Calif.

PRESIDENTIAL RECEPTION

The Reception will follow immediately after the program. Newly inducted Fellows should sign the Roster and secure their Fellowship Certificates during the interim between the Convocation and the Reception.

SIXTH GENERAL SESSION

Thursday Afternoon, February 9, 1933
2:00 o'Clock

WINDSOR HALL

Presiding Officer
Noble Wiley Jones,* Portland, Ore.

1. The Nervous Patient.
   George C. Hale,* London, Ont.
2. Schizophrenia from the Physiological Point of View.
   R. G. Hoskins, Boston, Mass.
   (Guest)

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*F.A.C.P.

3. The Evidence for a Cerebral Vascular Mechanism in Epilepsy.
   Wilder Penfield, Montreal, Que.
   (Guest)
4. The Relationship of the Autonomic Nervous System to General Medicine.
   Thomas P. Sprunt,* Baltimore, Md.
5. The Internist as His Own Psychiatrist.
   Alfred Stengel,† Philadelphia, Pa.
6. Experimental Uremia.
   B. O. Raulston,* Los Angeles, Calif.
7. The Management of Edema.
   Charles A. Elliott,* Chicago, Ill.
8. A Study of the Correlations between Physical Aspects of the Body and Disease Susceptibility.
   Walter Freeman,* Washington, D.C.
9. The Treatment of Chronic Intractable Asthma with Pollen Extracts.
   George L. Waldbott,* Detroit, Mich.

The Annual General Business Meeting of the College will be held immediately after the last paper. All Masters and Fellows are urged to be present. Official reports from the Executive Secretary and Treasurer will be read; new Officers, Regents and Governors will be elected, and the President-Elect, Dr. George Morris Piersol, will be inducted into office.

Thursday Evening, 7:30 o'Clock
WINDSOR HALL

THE ANNUAL BANQUET OF THE COLLEGE
(Procure Tickets at the Registration Bureau)

Toastmaster: Charles F. Martin,† Montreal, Que., Dean, Faculty of Medicine, McGill University.

Address: "The Waste Spaces of Modern Education."
Dr. Stephen Leacock, Montreal, Que., William Dow Professor of Political Economy, McGill University.

FINAL GENERAL SESSION
Friday Afternoon, February 10, 1933
2:00 o'Clock

WINDSOR HALL
Presiding Officer
George Morris Piersol,* Philadelphia, Pa.

1. Evaluation of Various Types of Therapy in Chronic Arthritis Based on Results in One Thousand Cases.
   W. Paul Holbrook,* Tucson, Ariz.
2. Research in Electrocardiography.
   William Reid,* Boston, Mass.
3. A Standard Test for Measuring Blood Pressure Variability: Its Significance as an Index of Prehypertensive States.
   George E. Brown,* Rochester, Minn.
4. Chronic Arterial Occlusion of the Extremities.
   Duncan Graham, Toronto, Ont.
   (Guest)
5. The Protean Nature of Subacute Bacterial Endocarditis.
   John H. Musser,* New Orleans, La.

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†M.A.C.P. *F.A.C.P.

6. Clinical and Experimental Observations upon the Heart in Hyperthyroidism.
   E. Cowles Andrus,* Baltimore, Md.
7. The Diagnosis and Medical Treatment of Angina Pectoris.
   Paul D. White,* Boston, Mass.
8. Experimental and Clinical Studies on the Surgical Treatment of Angina Pectoris.
   James C. White, Boston, Mass.
   (Guest)
9. Pulsus Alternans.
   John E. Greiwe,* Cincinnati, Ohio.
10. Aortic Stenosis, a Clinical and Pathological Consideration.
    Louis F. Bishop, Jr.,* New York, N.Y.

SPECIAL CLINICS AND DEMONSTRATIONS

Clinics and demonstrations will be held in the forenoons from 9:00 to 12:00 daily, Tuesday to Friday, inclusive.

Tickets will be required for each and every one of the special clinics, ward rounds and demonstrations. The co-operation of everyone in securing his clinic tickets will assist greatly in distributing the attendance according to the capacity of each program. It is self-evident that a ward round arranged for twenty-five will lose its value for all if forty or fifty are present. Ticket registration naturally is the only effective method of keeping the attendance within the capacities indicated.

To all members of the College, registration blanks for the clinics and demonstrations are distributed with the official program. These registration blanks should be filled out and returned to the Executive Secretary at once. Reservations by mail cannot be made after January 20, but reservations may be made in person at the Registration Bureau on the evening preceding any clinic day. *Guests will kindly register for clinics at the Registration Bureau upon arrival at Montreal.*

A-I

Tuesday, February 7, 1933

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Medical Theatre
(Capacity—100)

9:00- 9:45 Metabolic Aspects of Progressive Muscular Dystrophy.
W. S. McCann, Rochester, N.Y.

9:45-10:30 Treatment of Complications in Diabetes Mellitus.
E. H. Mason.

10:30-11:15 X-Ray Examination of the Heart.
T. Homer Coffen, Portland, Ore.

11:15-12:00 Therapeusis of Acute Circulatory Failure.
G. R. Brow.

A-II

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Surgical Theatre)
(Capacity—150)

9:00- 9:45 Peripheral Vascular Disease.
Mark Kaufmann.

9:45-10:30 Visceral Pain.
F. A. C. Scrimger.

10:30-11:15 Treatment of Pain in Buerger's Disease.
James C. White, Boston, Mass.

11:15-12:00 Lesions Due to Scalenal Pressure and Their Treatment.
William V. Cone.

Tuesday, February 7, 1933 (Continued)

A-III

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Nurses' Theatre
(Capacity—250)

9:00- 9:45 Syphilitic Heart Disease.
John H. Musser, New Orleans, La.

9:45-10:30 Thoracic Aneurysm.
Reginald Fitz, Boston, Mass.

10:30-11:15 Pathogenesis of the Symptom Complex of Tabes.
C. K. Russel.

11:15-12:00 Treatment of Cardiovascular Syphilis.
E. Cowles Andrus, Baltimore, Md.

A-IV

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward B
(Capacity—15)

9:00- 9:45 Bedside Clinic: The Common Cold.
W. Blair Stewart, Atlantic City, N.J.

9:45-10:30 Bedside Clinic: Sinusitis and Asthma.
A. T. Henderson.

10:30-11:15 Bedside Clinic: Chronic Arthritides.
W. Paul Holbrook, Tucson, Ariz.

11:15-12:00 Bedside Clinic: Neurological Clinic.
Arthur W. Young.

A-V

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward D
(Capacity—50)

9:00-11:30 A selected group of interesting cases will be continuously demonstrated for all members who may be interested to examine them between these hours.

A-VI

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward K
(Capacity—15)

9:00-10:00 Bedside Clinic: Metabolism in Bone Diseases.
W. de M. Scriver.

10:00-11:00 Bedside Clinic: Myxoedema.
David P. Barr, St. Louis, Mo.

A-VII

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Medical Laboratories
(Capacity—15)

11:00-12:00 Studies in Biochemistry.
1. Fat Digestion and Absorption.
A. Krakower.

Tuesday, February 7, 1933 (Continued)

2. Blood Fats and Their Variations.
   David Slight.
3. The Liver and Pancreas in Fat Metabolism.
   Mrs. Venning.
4. Analytical Biochemical Methods.
   R. U. Harwood.

B-I

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Surgical Theatre
(Capacity—200)

9:00- 9:45 Thoracic Pain.
C. A. Peters.

9:45-10:30 Bronchiectasis.
James Alex. Miller, New York, N.Y.

10:30-11:15 Pick's Disease.
Paul D. White, Boston, Mass.

11:15-12:00 Irradiation Treatment of Cancer about the Mouth.
George E. Pfahler, Philadelphia, Pa.

B-II

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Out-door Theatre
(Capacity—30)

9:00- 9:45 Cardiovascular Renal Syndrome.
G. C. Hale, London, Ont.

9:45-10-30 Asthma.
H. E. MacDermot.

10:30-11:15 Oxygen Therapy.
A. M. Burgess, Providence, R.I.

11:15-12:00 Stricture of Oesophagus.
R. E. Hodge.

B-III

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Pathological Theatre
(Capacity—60)

10:30-12:00 Pathological Conference.
J. E. Pritchard.

B-IV

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward A
(Capacity—50)

9:00-10:00 Ward Demonstration: Heart Disease in Pregnancy.
D. Grant Campbell.

10:00-11:00 Ward Demonstration: Placental Extracts in Gynecology.
A. D. Campbell.

Tuesday, February 7, 1933 (Continued)

B-V

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward C
(Capacity—50)

9:00-10:30 Ward Rounds.
A. H. Gordon.

10:30-12:00 Simultaneous Record of Heart Beat and Heart Sounds.
C. C. Birchard and Staff.

B-VI

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward E
(Capacity—50)

9:00-10:00 Ward Demonstration: Selected Cases of Skin Lesions.
F. J. Burgess.

10:00-11:00 Ward Demonstration: Essential Hypertension.
Joseph H. Barach, Pittsburgh, Pa.

C

McGILL UNIVERSITY MEDICAL SCHOOL
Biological Building
Department of Pharmacology, Fifth Floor
(Capacity—75)

9:00- 9:30 Moving Picture Film of Coronary Blood Flow.
R. L. Stehle.

9:30-10:00 Action of Pituitary Extract on Different Portions of the Gastro-intestinal Tract.
K. I. Melville.

10:00-10:30 Uric Acid Eliminants.
Hermann Schroeder.

10:30-10:45 Experimental Demonstration of the Effects of Coronary Constriction.
R. L. Stehle.

10:45-11:00 Chronic Mercury Poisoning.
K. I. Melville.

11:00-11:30 Moving Picture Film of Coronary Blood Flow.
R. L. Stehle.

D

McGILL UNIVERSITY MEDICAL SCHOOL
Pathological Institute
(3775 University St.)
Lecture Theatre
(Capacity—125)

9:00- 9:45 Bronchogenic Carcinoma (A Clinical, Bronchoscopic and Pathological Study).
L. H. Clerf and B. L. Crawford, Philadelphia, Pa.

9:45-10:30 Vegetal Foreign Bodies in the Bronchi.
D. H. Ballon.

10:30-11:15 Some Features in the Pathology of Coronary Disease of the Heart.
Oskar Klotz, Toronto, Ont.

11:15-12:00 Hemopoietic Effect of Nuclear Extractives Obtained from the Red Blood Cells of the Fowl.
Noble Wiley Jones, Portland, Ore.

Tuesday, February 7, 1933 (Continued)

E-I

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Clinical Theatre
(Capacity—150)

9:00- 9:45 Title to be supplied later.
E. Rist, Paris, France.
9:45-10:30 Cardiac Insufficiency.
A. LeSage.
10:30-11:15 Electrocardiography in Cardiac Insufficiency.
A. de Guise.
11:15-12:00 Radiology in Cardiac Disease.
A. Laquerrière.

E-II

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Out-Door Department
(Capacity—50)

10:00-12:00 Demonstration of Cases in Dermatology and Syphilis.
Alberic Marin and Assistants.

E-III

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Out-Door Department

10:00-12:00 Neurological Clinic.
Jean Saucier and Roma Amyot.

E-IV

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Medical Wards
(Capacity—15)

10:00-12:00 Bedside Clinics.
E. P. Benoit and Assistants.

F-I

HOTEL DIEU
(65 Pine Avenue, West)
Clinical Theatre
(Capacity—150)

9:00- 9:45 Gastro-intestinal Clinic.
Frank Smithies, Chicago, Ill.
9:45-10:30 Treatment and Prevention of Congestive Cardiac Failure.
J. E. Dubé.
10:30-11:15 Collapse Therapy in Pulmonary Tuberculosis.
J. P. Dworetzky, Liberty, N.Y.
11:15-12:00 Spontaneous Pneumothorax.
Guy Hamel.

Tuesday, February 7, 1933 (Continued)

F-II

HOTEL DIEU
(65 Pine Avenue, West)
Medical Wards
(Capacity—15)

9:00-10:00 Bedside Clinic.
J. R. Pepin.
10:00-11:00 Bedside Clinic: Treatment of Peptic Ulcer.
Logan Clendening, Kansas City, Mo.
11:00-12:00 Bedside Clinic: Cardiac Clinic.
E. Tetreault.

G-I

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Medical Theatre
(Capacity—100)

9:00-10:00 Tuberculosis in Children.
Horton Casparis, Nashville, Tenn.
10:00-11:30 Clinical and Pathological Features of Rheumatic Fever in Children.
H. B. Cushing and L. J. Rhea.
11:30-12:00 An Estimate of the Value of Certain Observed Phenomena in Determining the Activity of Rheumatic Infection.
R. R. Struthers.

G-II

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Baby Ward
(Capacity—15)

9:00-10:30 Ward Rounds.
Alton Goldbloom.

G-III

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Medical Ward
(Capacity—15)

10:30-12:00 Ward Rounds.
L. M. Lindsay.

H

HÔPITAL SAINTE JUSTINE
(6055 St. Denis St.)
No Program on Tuesday

I-I

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Department of Anatomy, Third Floor
No Program on Tuesday

Tuesday, February 7, 1933 (Continued)

I-II

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Osler Library, Third Floor
(Capacity—75)

9:30- 1:00 and 2:30- 5:00 The Osler Library will be open between these hours, when Sir William Osler's collection may be inspected. A special exhibit of books famous in the history of Medicine and Science has been arranged. The Librarian, Dr. W. W. Francis, will be present to receive all visitors.

I-III

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Pathological Museum, Second Floor
(Capacity—75)

Special exhibits will be set out consisting of:

a) Collection on the Clinical Classification of Congenital Heart Disease recently presented at the Centenary Meeting of the British Medical Association:

b) Representative series from the Medical Historical Museum. These will include (1) Sir William Osler's Canadian Pathological collection, consisting of some 150 specimens, with its Bibliography; (2) other special exhibits illustrative of general Medical History.

Maude E. Abbott.

Wednesday, February 8, 1933

A-I

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Medical Theatre
(Capacity—100)

9:00- 9:45 Heart Disease from the Obstetrician's Point of View.
John R. Fraser.

9:45-10:30 Handling of Heart Disease in Pregnancy.
S. Marx White, Minneapolis, Minn.

10:30-11:15 Factors Operative in Circulatory Failure.
Jonathan C. Meakins.

11:15-12:00 Some Aspects of the Etiology of Hematuria.
D. W. MacKenzie.

A-II

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Surgical Theatre
(Capacity—150)

9:00- 9:45 Physiology of Pulmonary Collapse.
Ronald V. Christie.

9:45-10:30 Results and Causes of Failure in Collapse Therapy.
Charles H. Cocke, Asheville, N.C.

Wednesday, February 8, 1933 (Continued)

10:30-11:15 Indications for Surgical Interference in Pulmonary Tuberculosis.
Lawrason Brown, Saranac Lake, N.Y.
11:15-12:00 Results of Surgical Treatment of Pulmonary Tuberculosis.
E. W. Archibald.

A-III

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Nurses' Theatre
(Capacity—250)

9:00-10:00 Neurogenic Factors in Epilepsy.
Stanley Cobb, Boston, Mass.
10:00-11:00 A Discussion of the Etiology and Treatment of Epilepsy.
Henry Rawle Geyelin, New York, N.Y.
11:00-12:00 Focal Epilepsy—Its Diagnosis and Treatment.
Wilder Penfield.

A-IV

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward B
(Capacity—15)

9:00- 9:45 Bedside Clinic: Blood Transfusion (A Demonstration)
Henry F. Stoll, Hartford, Conn.
9:45-10:30 Bedside Clinic.
W. F. Hamilton.
10:30-11:15 Bedside Clinic: Acute Pulmonary Tuberculosis.
J. R. Byers.
11:15-12:00 Bedside Clinic: Gastro-intestinal Clinic.
C. J. Tidmarsh.

A-V

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward D
(Capacity—50)

9:00-11:30 Demonstration of Dermatological Cases.
Philip Burnett.

A-VI

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward K
(Capacity—15)

9:00-10:00 Bedside Clinic: Atypical Renal Glycosuria.
E. H. Mason.
10:00-11:00 Bedside Clinic: Diabetes.
Joseph H. Barach, Pittsburgh, Pa.

Wednesday, February 8, 1933 (Continued)

A-VII

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Medical Laboratories
(Capacity—15)

11:00-12:00 Demonstrations in Cardiac Physiology:

1. The Continuous Registration of the Heart and Respiratory Rate in Man.
   Ronald V. Christie and G. H. Shepherd.
2. Studies of the Electrocardiographic "T" Wave.
   G. R. Brow and D. V. Holman.
3. Animal Studies of Acute Heart Failure.
   Gerald Evans.
4. Visualization of Liver and Spleen by X-Ray with Thorium Dioxide.
   R. Gottlieb.

B-I

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Surgical Theatre
(Capacity—200)

9:00- 9:45 Liver Function and Laboratory Tests in Biliary Disease.
T. B. Magath, Rochester, Minn.

9:45-10:30 X-Ray versus Clinical Diagnosis in Biliary Disease.
W. L. Ritchie.

10:30-11:15 The Management of Hepatic Disease.
Charles A. Elliott, Chicago, Ill.

11:15-12:00 Surgical Aspects of Diseases of the Biliary Passages.
A. T. Bazin.

B-II

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Out-Door Theatre
(Capacity—30)

9:00- 9:45 Cardiac Clinic.
Wm. D. Reid, Boston, Mass.

9:45-10:30 Renal Glycosuria with Acidosis.
A. F. Fowler.

10:30-11:15 Splenomegaly.
E. H. Falconer, San Francisco, Calif.

11:15-12:00 Problems in Hematology.
E. S. Mills.

B-III

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Pathological Theatre
(Capacity—60)

10:30-12:00 Pathological Conference.
L. J. Rhea.

B-IV

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward A
No program on Wednesday.

Wednesday, February 8, 1933 (Continued)

B-V

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward C
(Capacity—50)

10:30-12:00 Simultaneous Record of Heart Beat and Heart Sounds.
C. C. Birchard and Staff.

B-VI

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward E
(Capacity—50)

9:00-10:00 Ward Demonstration: Lead Poisoning.
Maurice C. Pincoffs, Baltimore, Md.

10:00-11:00 Ward Demonstration: Neurological Clinic.
F. H. MacKay.

C

McGILL UNIVERSITY MEDICAL SCHOOL
Biological Building
Department of Physiology, Fourth Floor
(Capacity—75)

9:00- 9:15 Experiments on the Labyrinth in Relation to Posture.
W. J. McNally and John Tait.

9:15- 9:45 Experiments on Hearing in Conditioned Cats and Dogs.
S. Dworkin and G. F. Sutherland.

9:45-10:00 Experiments on Tremor Sense in Conditioned Cats.
S. Dworkin.

10:00-10:15 Electrical Records from the Eighth Nerve.
D. A. Ross.

10:15-10:30 Mechanism of Natural Arrest of Hemorrhage from a Wound.
John Tait.

10:30-12:00 Experiments to Demonstrate the Modern Conceptions of Gastric Secretion and Their Bearing on Gastric Digestion.
B. P. Babkin and Assistants.

D

McGILL UNIVERSITY MEDICAL SCHOOL
Pathological Institute
(3775 University St.)
Lecture Theatre
(Capacity—125)

9:00- 9:40 The Heart Beat and Electrocardiograph (Moving Picture).
L. M. Hurxthal, Boston, Mass.

9:45-10:00 Syndrome of the Superior Cerebellar Artery (Moving Picture).
C. K. Russel.

10:00-10:45 Chronic Arthritis (Moving Picture).
W. Paul Holbrook, Tucson, Ariz.

E-I

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Clinical Theatre
(Capacity—150)

9:00- 9:45 Pathological Anatomy of Chronic Gastritis.
Pierre Masson.

Wednesday, February 8, 1933 (Continued)

9:45-10:30 Symptomatology of Peptic Ulcer.
E. P. Benoit.
10:30-11:15 The Radiological Diagnosis of Peptic Ulcer.
A. Laquerrière.
11:15-12:00 The Treatment of Peptic Ulcer.
H. Gelinas.

E-II

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Out-Door Department
No Program on Wednesday

E-III

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Out-Door Department
(Capacity—10)

10:00-12:00 Neurological Clinic.
Edgar Langlois and Assistants.

E-IV

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Medical Wards
(Capacity—15)

10:00-12:00 Bedside Clinics.
A. LeSage and Assistants.

F-I

HOTEL DIEU
(65 Pine Avenue, West)
Clinical Theatre
(Capacity—150)

9:00- 9:45 Title to be supplied later.
E. Rist, Paris, France.
9:45-10:30 General Survey of Pyelitis.
Oscar Mercier.
10:30-11:15 Duodenal Ulcer.
Lay Martin, Baltimore, Md.
11:15-12:00 X-Ray Demonstration.
Leo Pariseau.

F-II

HOTEL DIEU
(65 Pine Avenue, West)
No Program on Wednesday

G-I

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Medical Theatre
(Capacity—100)

9:00-10:00 1. Coeliac Disease.
2. Bronchiectasis and Asthma.
Alan Brown, Toronto, Ont.

Wednesday, February 8, 1933 (Continued)

10:00-10:30 Relation of Sinus Infection to Respiratory Diseases in Infancy and Childhood.
A. B. Chandler.
10:30-11:15 Renal Dwarfism.
L. M. Lindsay.
11:15-12:00 A Case of Osteomalacia with Cloudiness of the Cornea.
S. Graham Ross.

G-II

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Baby Ward
(Capacity—15)

9:00-10:30 Ward Rounds.
H. P. Wright.

G-III

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Medical Ward
(Capacity—15)

10:30-12:00 Ward Rounds.
H. B. Cushing.

H

HÔPITAL SAINTE JUSTINE
(6055 St. Denis St.)
Clinical Theatre
(Capacity—100)

9:00- 9:45 Asthma in Children.
Horton Casparis, Nashville, Tenn.
9:45-10:30 Les état de dénutrition du nourrisson. (The State of Undernourishment in Infants).
Gaston Lapierre.
10:30-11:15 Le problème de l'épilepsie infantile. (The Problem of Infantile Epilepsy.)
J. A. Lussier.
11:15-12:00 Le tétanie infantile. (Infantile Tetany.)
Henri Baril.

I-I

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Department of Anatomy, Third Floor
No Program on Wednesday.

I-II

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Osler Library, Third Floor
(Capacity—75)

9:30- 1:00 and 2:30- 5:00 The Osler Library will be open between these hours, when Sir William Osler's collection may be inspected. A special exhibit of books famous in the history of Medicine and Science has been arranged.
The Librarian, Dr. W. W. Francis, will be present to receive all visitors.

Wednesday, February 8, 1933 (Continued)

I-III

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Pathological Museum, Second Floor
(Capacity—75)

Special Exhibits will be set out consisting of:

a) Collection on the Clinical Classification of Congenital Heart Disease recently presented at the Centenary Meeting of the British Medical Association;

b) Representative series from the Medical Historical Museum. These will include (1) Sir William Osler's Canadian Pathological collection, consisting of some 150 specimens, with its Bibliography; (2) Other special exhibits illustrative of general Medical History.

Maude E. Abbott.

Thursday, February 9, 1933

A-I

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Medical Theatre
(Capacity—100)

9:00- 9:45 Types of Chronic Rheumatism.
Ralph Kinsella, St. Louis, Mo.

9:45-10:30 Intravenous Vaccine Therapy in Chronic Arthritis.
W. B. Rawls, New York, N.Y.

10:30-11:15 Chronic Intractable Asthma.
G. L. Waldbott, Detroit, Mich.

11:15-12:00 Diagnostic Clinic.
Logan Clendening, Kansas City, Mo.

A-II

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Surgical Theatre
(Capacity—150)

9:00- 9:45 Hypertension and Cerebral Phenomena.
Alfred Gordon, Philadelphia, Pa.

9:45-10:30 Angina Pectoris.
J. B. Wolffe, Philadelphia, Pa.

10:30-11:15 Jaundice in Cardiac Disease.
Alfred Stengel, Philadelphia, Pa.

11:15-12:00 Diuretics.
D. Sclater Lewis.

A-III

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Nurses' Theatre
(Capacity—250)

9:00- 9:45 The Relation of Emotional Factors to Thyroid Disorders.
James H. Means, Boston, Mass.

Thursday, February 9, 1933 (Continued)

9:45-10:30 The Importance of Mental Aspects in the Etiology and Treatment of Tuberculosis.
Lawrason Brown, Saranac Lake, N.Y.

10:30-11:15 The Psychiatric Factors in the Causation of Gastro-intestinal Disorders.
W. C. Alvarez, Rochester, Minn.

11:15-12:00 Emotional Factors in Organic Disease.
Franz Alexander, Chicago, Ill.

A-IV

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward B
(Capacity—50)

9:00-11:30 A selected group of interesting cases will be continuously demonstrated for all members who may be interested to examine them between these hours.

A-V

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward D
(Capacity—15)

9:00- 9:45 Bedside Clinic: Chronic Chlorosis.
William B. Castle, Boston, Mass.

9:45-10:30 Bedside Clinic.
C. F. Moffatt.

10:30-11:15 Bedside Clinic: Clinical Diagnosis of Cardio-arrhythmias.
Wm. D. Reid, Boston, Mass.

11:15-12:00 Bedside Clinic: Peptic Ulcer.
C. G. Sutherland.

A-VI

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward K
(Capacity—15)

9:00-10:00 Bedside Clinic: Obesity.
James S. McLester, Birmingham, Ala.

10:00-11:00 Bedside Clinic: Toxic Adenoma of the Thyroid.
Henry M. Thomas, Jr., Baltimore, Md.

A-VII

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Medical Laboratories
(Capacity—15)

11:00-12:00 Demonstrations in Respiratory Physiology:

1. The Measurement of Lung Volume without Forced Breathing.
Ronald V. Christie and C. A. McIntosh.
2. Variations in Lung Volume and its Functional Significance in Disease.
   (a) Normals,
   (b) Emphysema,
   (c) Pneumothorax, Phrenicotomy and Thoracoplasty,
   (d) Lungectomy,
   (e) Respiratory Neurosis.
   Ronald V. Christie and C. A. McIntosh.

Thursday, February 9, 1933 (Continued)

B-I

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Surgical Theatre
(Capacity—200)

9:00- 9:45 Diabetes.
E. P. Joslin, Boston, Mass.
9:45-10:30 Tuberculosis and Diabetes.
W. R. Kennedy.
10:30-11:15 The Fundas Oculi in Diabetes Mellitus.
S. H. McKee.
11:15-12:00 The Treatment of Diabetes.
Henry Rawle Geyelin, New York, N.Y.

B-II

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Out-Door Theatre
(Capacity—30)

9:00- 9:45 Poliomyelitis.
P. N. MacDermot.
9:45-10:30 Encephalitis.
Lorne C. Montgomery.
10:30-11:15 Virus Diseases.
O. H. Perry Pepper, Philadelphia, Pa.
11:15-12:00 A Discussion of the Use of Vaccine in Chronic Arthritis.
Sydney R. Miller, Baltimore, Md.

B-III

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Pathological Theatre
(Capacity—60)

10:30-12:00 Pathological Conference: Malignancy and Infection of the Genito-urinary Tract.
F. S. Patch.

B-IV

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward A
No Program on Thursday.

B-V

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward C
(Capacity—50)

9:00-10:00 Circulatory Disturbances of the Extremities.
George E. Brown, Rochester, Minn.
10:00-11:00 Thrombo-angiitis Obliterans.
Thomas P. Sprunt, Baltimore, Md.
11:00-12:00 Demonstration of Tests for Vascular Disease of Extremities.
C. W. Fullerton.

Thursday, February 9, 1933 (Continued)

B-VI

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward E
(Capacity—50)

9:00-10:00 Ward Demonstration: Discussion on the Control of Angina Pectoris Attacks in Persons who have Insufficient Pancreatic Function.
Anthony Bassler, New York, N.Y.

10:00-11:00 Ward Demonstration: Chronic Nephritis.
George Morris Piersol, Philadelphia, Pa.

C

McGILL UNIVERSITY MEDICAL SCHOOL
Biological Building
Department of Biochemistry, Third Floor
(Capacity—75)

9:00-12:00 Demonstration of a Series of Experiments Dealing With Hormone Research:
(a) Sex Hormones,
(b) Parathyroid Hormones,
(c) Results of Hypophysectomy in the Rat and Results of Various Methods of Treatment.
J. B. Collip and Assistants.

D

McGILL UNIVERSITY MEDICAL SCHOOL
Pathological Institute
(3775 University St.)
Lecture Theatre
(Capacity—125)

9:00- 9:45 Physiology and Pathology of the Carotid Gland.
Ronald V. Christie and W. H. Chase.

9:45-10:30 Hemolytic Anemia in Generalized Carcinomatosis of Bone.
T. R. Waugh.

10:30-12:00 Staff Pathological Conference.
Horst Oertel.

E-I

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Clinical Theatre
(Capacity—150)

9:00- 9:45 Title to be supplied later.
E. Rist, Paris, France.

9:45-10:30 Unusual Onsets of Disseminated Sclerosis.
Jean Saucier.

10:30-11:15 Atypical Forms of Syringomyelia.
Roma Amyot.

11:15-12:00 Treatment of Cutaneous Basal-cell Epithelioma.
Alberic Marin.

E-II

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Out-Door Department
(Capacity—50)

10:00-12:00 Demonstration of Cases in Dermatology and Syphilis.
Alberic Marin and Assistants.

Thursday, February 9, 1933 (Continued)

E-III

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Out-Door Department
No Program on Thursday.

E-IV

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Medical Wards
(Capacity—15)

10:00-12:00 Bedside Clinics.
E. P. Benoit and Assistants.

F-I

HOTEL DIEU
(65 Pine Avenue, West)
Clinical Theatre
(Capacity—150)

9:45-10:30 Relation of the Laboratory to Clinical Medicine.
George Baril.
10:30-11:15 Arthritis.
S. M. Alter, Los Angeles, Calif.
11:15-12:00 Dietetic Treatment of Diabetes.
J. R. Pepin.

F-II

HOTEL DIEU
(65 Pine Avenue, West)
Medical Wards
(Capacity—15)

9:00-10:00 Bedside Clinic: Nephritic Clinic.
J. E. Dubé
10:00-11:00 Bedside Clinic: Gastro-intestinal Clinic.
R. Gatien.
11:00-12:00 Bedside Clinic.
Guy Hamel.

G-I

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Medical Theatre
(Capacity—100)

9:00-12:00 Clinical and Laboratory Symposium on Lead Poisoning in Children.

1. *Introduction:* H. B. Cushing.
   Reasons for apparent increase in frequency of lead poisoning. New methods of diagnosis. Possible means of control.
2. *X-Ray Demonstration:* A. E. Childs.
   Changes in growing ends of bones caused by lead. Demonstration of lead in intestines.
3. *Pathological Changes:* L. J. Rhea.
   Character of bone changes, changes in nervous system.
4. *Clinical Manifestations:* H. S. Mitchell.
   Presentation of series of cases, illustrating various types of lead poisoning in children.

Thursday, February 9, 1933 (Continued)

5. *Chemistry of Lead Poisoning:* I. M. Rabinowitch.
Methods of detection of lead in the body. Explanation of deposition of lead in the body and its removal.
6. *Treatment:* S. Graham Ross.
Dietary and medicinal methods of fixation of lead in body and deleading. Methods for relief of symptoms.

G-II

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Baby Ward
(Capacity—15)

9:00-10:30 Ward Rounds.
Alan Brown, Toronto, Ont.

G-III

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Medical Ward
(Capacity—15)

10:30-12:00 Ward Rounds.
A. B. Chandler.

H

HÔPITAL SAINTE JUSTINE
(6055 St. Denis St.)
Clinical Theatre
No Program on Thursday.

I-I

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Department of Anatomy, Third Floor
No Program on Thursday.

I-II

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Osler Library, Third Floor
(Capacity—75)

9:30- 1:00 and 2:30- 5:00 The Osler Library will be open between these hours, when Sir William Osler's collection may be inspected. A special exhibit of books famous in the history of Medicine and Science has been arranged. The Librarian, Dr. W. W. Francis, will be present to receive all visitors.

I-III

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Pathological Museum, Second Floor
(Capacity—75)

Special Exhibits will be set out consisting of:

Thursday, February 9, 1933 (Continued)

a) Collection on the Clinical Classification of Congenital Heart Disease recently presented at the Centenary Meeting of the British Medical Association;

b) Representative series from the Medical Historical Museum. These will include (1) Sir William Osler's Canadian Pathological colection, consisting of some 150 specimens, with its Bibliography; (2) Other special exhibits illustrative of general Medical History.

Maude E. Abbott.

Friday, February 10, 1933

A-I

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Medical Theatre
(Capacity—100)

9:00- 9:45 Diverticulitis.
R. H. M. Hardisty.

9:45-10:30 X-Ray Diagnosis of Diverticula of the Gastro-intestinal Tract.
E. C. Brooks.

10:30-11:15 Progress in the Management of Various Types of Colitis.
J. A. Bargen, Rochester, Minn.

11:15-12:00 Jaundice in Diagnosis.
Lay Martin, Baltimore, Md.

A-II

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Surgical Theatre
(Capacity—150)

9:00- 9:45 Erythema Nodosum and Tuberculosis.
H. B. Cushing.

9:45-10:30 Pulmonary Neoplasms.
Harlow Brooks, New York, N.Y.

10:30-11:15 Differential Diagnosis of Congenital Heart Disease, with Illustrative Cases.
Maude E. Abbott.

11:15-12:00 X-Ray Diagnosis of Bone Lesions.
A. Howard Pirie.

A-III

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Nurses' Theatre
(Capacity—250)

9:00- 9:45 Pernicious Anemia.
Cyrus C. Sturgis, Ann Arbor, Mich.

9:45-10:30 Neutropenia.
J. Kaufmann.

10:30-11:15 Monocytic Leukemia.
Thomas P. Sprunt, Baltimore, Md.

11:15-12:00 Myelotoxic Anemia.
R. Gottlieb.

Friday, February 10. 1933 (Continued)

A-IV

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward B
(Capacity—50)

9:00-11:30 A selected group of interesting cases will be continuonsly demonstrated for all members who may be interested to examine them between these hours.

A-V

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward D
(Capacity—15)

9:00- 9:45 Bedside Clinic.
W. F. Hamilton.

9:45-10:30 Bedside Clinic: Cardiac Asthma.
Maurice C. Pincoffs, Baltimore, Md.

10:30-11:15 Bedside Clinic: Diagnostic Clinic on Hepatic Enlargement.
Duncan Graham, Toronto, Ont.

11:15-12:00 Bedside Clinic.
D. Sclater Lewis.

A-VI

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Ward K
(Capacity—15)

9:00-10:00 Bedside Clinic:Tetany.
David P. Barr, St. Louis, Mo.

10:00-11:00 Bedside Clinic: The Diabetic Child.
E. H. Mason.

A-VII

ROYAL VICTORIA HOSPITAL
(Pine Avenue, West)
Neuro-pathological Laboratories
(Capacity—15)

11:00-12:00 Demonstration of Neuro-pathological Material.
W. V. Cone, Lyle Gage and Assistants.

B-I

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Surgical Theatre
(Capacity—200)

9:00- 9:45 Clinical Aspects of Hyperthyroidism.
Roger I. Lee, Boston, Mass.

9:45-10:30 Pitfalls in Interpretation of Tests for Basal Metabolism.
I. M. Rabinowitch.

10:30-11:15 The Present Status of the Medical Treatment of Hyperthyroidism.
James H. Means, Boston, Mass.

11:15-12:00 Surgical Aspects of Hyperthyroidism.
E. M. Eberts.

Friday, February 10. 1933 (Continued)

B-II

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Out-Door Theatre
(Capacity—30)

9:00- 9:45 Arteriosclerotic Heart Disease.
F. M. Smith, Iowa City, Iowa.
9:45-10:30 Aortic Valvular Disease.
L. F. Bishop, Jr., New York, N.Y.
10:30-11:15 Digitalis Therapy.
H. N. Segall.
11:15-12:00 Quinidine Therapy.
Neil Feeney.

B-III

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Pathological Theatre
(Capacity—60)

10:30-12:00 Pathological Conference.
L. J. Rhea.

B-IV

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward A
No Program on Friday.

B-V

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward C
(Capacity—50)

9:00-10:00 Ward Demonstration: Silicosis.
J. G. Browne.
10:00-11:00 Ward Demonstration: Delayed Development of Pneumoconiosis.
P. H. Pierson, San Francisco, Calif.
11:00-12:00 Ward Demonstration: Pneumothorax.
J. B. Ross.

B-VI

MONTREAL GENERAL HOSPITAL
(66 Dorchester St., East)
Ward E
(Capacity—50)

9:00-10:30 Ward Rounds.
C. P. Howard.

C

McGILL UNIVERSITY MEDICAL SCHOOL
Biological Building
No Program on Friday.

Friday, February 10, 1933 (Continued)

D

McGILL UNIVERSITY MEDICAL SCHOOL
Pathological Institute
(3775 University St.)
Lecture Theatre
(Capacity—125)

9:00-10:00 The Clinical Significance of Diphtheroid Bacilli; A Critical Analysis of 510 Positive Blood Cultures from 320 Patients.
R. H. Durham, Detroit, Mich.

10:00-11:00 A New Conception of the Pathology of Experimental Tuberculosis.
S. A. Petroff, Saranac Lake, N.Y.

11:00-12:00 Renal Cortical Necrosis.
W. de M. Scriver.

E-I

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Clinical Theatre
(Capacity—150)

9:00- 9:45 Lipoidic Nephrosis.
A. Leger.

9:45-10:30 Choleocystitis.
J. Albert Rouleau.

10:30-11:15 Choleocystography.
J. A. Mousseau.

11:15-12:00 Cholelithiasis.
Frank Smithies, Chicago, Ill.

E-II

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Out-Door Department
(Capacity—50)

10:00-12:00 Demonstration of Cases in Dermatology and Syphilis.
Alberic Marin and Assistants.

E-III

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Out-door Department
No Program on Friday.

E-IV

NOTRE DAME HOSPITAL
(1560 Sherbrooke St., East)
Medical Wards
(Capacity—15)

10:00-12:00 Bedside Clinics.
A. LeSage and Assistants.

Friday, February 10, 1933 (Continued)

F-I

HOTEL DIEU
(65 Pine Avenue, West)
Clinical Theatre
(Capacity—150)

9:00- 9:45 Title to be supplied later.
E. Rist, Paris, France.
9:45-10:30 External Causes of Ocular Muscle Deficiency.
P. E. Bousquet.
10:30-11:15 Cardiac Clinic.
Walter L. Bierring, Des Moines, Iowa.
11:15-12:00 Goitre.
Donald Hingston.

F-II

HOTEL DIEU
(65 Pine Avenue, West)
No Program on Friday.

G-I

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Medical Theatre
(Capacity—100)

9:00- 9:30 Diphtheria Immunization by Intracutaneous Methods.
Alton Goldbloom.
9:30-10:00 Simple Anemias of Infancy.
H. P. Wright.
10:00-10:30 Treatment of Congenital Lues.
A. K. Geddes.
10:30-11:00 Demonstration of Unusual Skin Diseases Encountered in Children.
L. P. Ereaux.
11:00-12:00 Demonstration of Neurological Cases.
A. W. Young.

G-II

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Baby Ward
(Capacity—15)

9:00-10:30 Ward Rounds.
R. R. Struthers.

G-III

CHILDREN'S MEMORIAL HOSPITAL
(1415 Cedar Avenue)
Medical Ward
(Capacity—15)

10:30-12:00 Ward Rounds.
S. Graham Ross.

Friday, February 10, 1933 (Continued)

H

HÔPITAL SAINTE JUSTINE
(6055 St. Denis St.)
Clinical Theatre
(Capacity—100)

9:00- 9:45 Broncho-pneumonies à Plasmode. (Malarial Broncho-pneumonia.)
Pierre Masson.

9:45-10:30 Le Vaccin B. C. G. (Vaccine B. C. G.).
J. A. Beaudouin.

10:30-11:15 Diagnostic des Cardiopathies Infantiles. (Diagnosis of Cardiopathies in Infants.)
Paul Letondal.

11:15-12:00 Le Diabète Infantile. (Infantile Diabetes.)
A. Dutilly.

I-I

McGILL UNIVERSITY MEDICAL SCHOOL
Medical Building
(3640 University St.)
Department of Anatomy, Third Floor
(Capacity—100)

9:00-10:00 Consideration of Referred Pain.
S. E. Whitnall.

10:00-11:00 The Neurogenic Factor in Gastric and Duodenal Ulcer.
J. Beattie.

11:00-12:00 The Demonstration of Preparations of the Nasal Accessory Sinuses.
H. E. MacDermot.

I-II

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Medical Building
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The Librarian, Dr. W. W. Francis, will be present to receive all visitors.

I-III

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Maude E. Abbott.

OBITUARIES

DOCTOR ALFRED LEFTWICH GRAY

Dr. Alfred Leftwich Gray (Fellow), died at his home in Richmond, Va., October 13, 1932, after an illness of eighteen months.

Dr. Gray was born October 2, 1873, at Palmyra, Va., and received his academic and medical training at the University of Virginia, from which he was graduated in 1897. In 1899 he joined the faculty of the University College of Medicine, where he served as Professor of Physiology from 1901 until that school was merged with the Medical College of Virginia in 1913. He was a pioneer in Roentgenology and in 1916 became Professor of Roentgenology in the Medical College of Virginia, a position he continued to fill until his death. In addition to teaching and private practice he was Roentgenologist to the Hospital Division of the Medical College of Virginia, St. Luke's Hospital and Pine Camp Hospital, and was Dean of the Medical College of Virginia from 1913 to 1919.

At the beginning of the World War Dr. Gray was commissioned Major in the Medical Reserve Corps and, as commanding officer, organized and conducted the Richmond School of Military Roentgenologists. He was an active member of numerous medical organizations and served as president of the Richmond Academy of Medicine, Medical Society of Virginia, American College of Roentgenology and American Roentgen Ray Society. He had beeen a Fellow of the American College of Physicians since 1920. While a recital of the posts he held indicates a life of accomplishment far beyond the ordinary, it fails to portray fully those qualities of mind and heart that will linger longest in the memories of those who knew him. To few, indeed, is it given to attain the degree of confidence and affection in which Dr. Gray was held by his fellow physicians. His ability, energy and sense of fairness marked him as a leader and he was chosen often to represent the various professional and educational organizations with which he was connected. Especially in times of stress, when men lose their heads and passion rules, his innate tact and sound judgment shone brilliantly. Of his time and talents he gave generously. To the hundreds of physicians and students with whom he labored he was ever the sympathetic friend and genial companion, who was always accessible and always willing to help.

In the passing of Dr. Gray the State has lost one of its most useful sons; the medical profession a most loyal and devoted member; and his associates a wise counsellor and faithful friend.

(Furnished by J. MORRISON HUTCHESON, M.D., F.A.C.P., Governor for Virginia)

DOCTOR EDWARD BATES BLOCK

Dr. Edward Bates Block (Fellow), Atlanta, Ga., died October 25, 1932; aged, fifty-eight years.

Dr. Block received his medical de-

gree from the University of Virginia Department of Medicine in 1895. Thereafter he was Assistant Resident Physician at Johns Hopkins Hospital from 1895 to 1897; Assistant Pathologist and Bacteriologist, University of Minnesota, 1897 to 1898; Assistant in Neurology at the University of Strassburg from 1898 to 1899; Volunteer Assistant, University of Prague, 1899 to 1900; Assistant Neurologist, Johns Hopkins Hospital, 1900 to 1901; Professor of Neurology and Psychiatry, Emory University School of Medicine, 1901 to the date of his death. He was also Visiting Neurologist to the Grady Memorial Hospital and Visiting Neurologist and Psychiatrist to the Wesley Memorial Hospital, both of Atlanta.

Dr. Block was the author of a large number of publications. He was an ex-President of the Fulton County (Ga.) Medical Society, ex-President of the Atlanta Neurological Association, a member of the Medical Association of Georgia, a member of the Southern Interurban Clinical Club, a member of the Southern Medical Association, a member of the American Neurological Association, a member of the Association for Research in Nervous and Mental Diseases, a member of the American Medical Association, a Fellow of the American Association for Advancement of Science, and had been a Fellow of the American College of Physicians since 1928.